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COMBINED THERMOANALYTICAL—MASS-SPECTROMETRIC INVESTIGATION OF CRUPODEX[R] DEXTRANOMER

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A cross-linked dextranomer, which is used as a wound drying and cleansing powder (Crupodex[R]), has been investigated by several thermoanalytical methods. First the TG, DTG and DTA characteristics were studied and compared with those of another product (Debrisan[R]), marketed earlier. The TG curves were also used for the examination of water uptake and the drying process. The traces of organic solvents (mainly ethanol) remaining from the manufacturing process were studied with a quadrupole mass-spectrometer coupled to a derivatograph. From the results of these experiments, several conclusions were drawn about the mechanism of water and solvent uptake.

Cross-linked dextran polymers (e.g. Debrisan[R]) have been widely used in the treatment of wounds of different origins since the middle of the seventies. The polymer continuously absorbs wound exudate and removes bacteria, thereby drying and cleansing wounds. Dextranomers cure wounds without crust formation and have no anaphylactogenic action [1–4]. Crupodex[R] is another product, with a similar structure and effect [5].

The powder consists of porous spherical beads built up from three-dimensional macromolecular chains, which are strongly hygroscopic. This porous network displays molecular sieve behaviour, i.e. molecules with a molecular weight above 5000 cannot enter the granules, but remain in the intergranular spaces. One of the most important characteristics of cross-linked dextran polymers is their water uptake: they can absorb a multiple of their own weight, undergoing swelling in the process. The absorbed water is bound in both the intragranular and the intergranular spaces.

Thermogravimetry is a suitable method for quantitative investigation of the processes of uptake and loss of water. In the present work, the optimum swelling

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and drying periods were determined from a comparison of the thermoanalytical curves of Debrisan^R and Crupodex^R. The distribution of the absorbed water and organic solvents (e.g. ethanol and isopropanol) used to manufacture the products was studied by means of a combined thermogravimetric–mass-spectrometric method.

Experimental

The preparations used in the experiments were products of Pharmacia, Sweden (Debrisan^R), and Biogal, Hungary (Crupodex^R).

The thermoanalytical measurements were made on a Derivatograph–1000 °C (MOM, Hungary) controlled by an LP 839 temperature controller (Chinoin, Hungary). The thermoanalytical–mass-spectrometric analyses were performed with a QMS–300 quadrupole mass-spectrometer coupled to a Derivatograph–1000 °C instrument [6].

Results and discussion

Comparison of thermal characteristics of Crupodex^R and Debrisan^R

The samples were swollen in water for 24 hours, after which TG, DTG and DTA measurements were carried out (see Fig. 1). Samples were heated at a rate of 10 deg/min up to 700°.

It can be seen from Fig. 1 that the two products behave almost identically. Water is released up to 240–260°, with a maximum rate at 140°. The water loss is 68% for Debrisan^R and 65% for Crupodex^R. Above 260°, the thermal degradation of the cross-linked structure takes place in two exothermic processes, at two characteristic temperatures: 375° and 550° for Debrisan^R, and 380° and 540° for Crupodex^R.

Investigation of water uptake

The water uptake capacity (expressed in ml/g) of the dextranomers is the volume of water in ml bound in the intragranular and intergranular spaces of 1 g of cross-linked dextranomer. The water-retaining capacity is given by the amount of water absorbed inside the granules. For Debrisan^R, it was determined by Emoto et al. [7] in the following way: the polymer was swollen in water for 24 hours, the intergranular water was then removed by centrifuging, and the dextranomer was

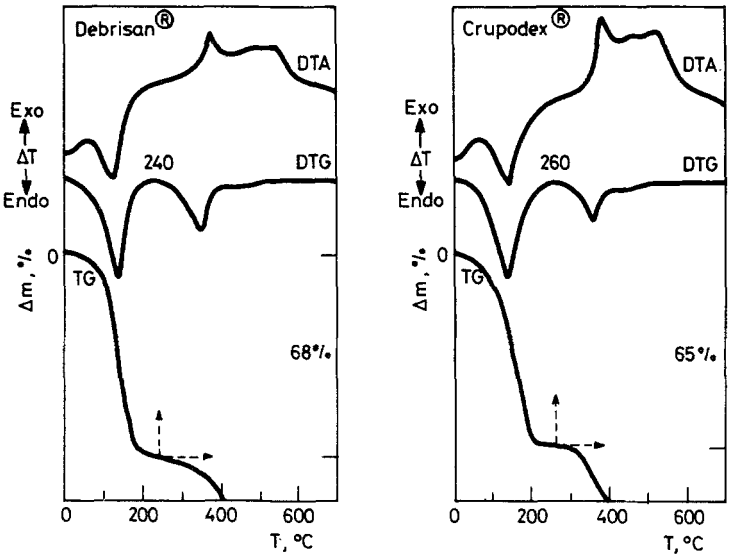

Fig. 1 TG, DTG and DTA curves of Crupodex^R and Debrisan^R

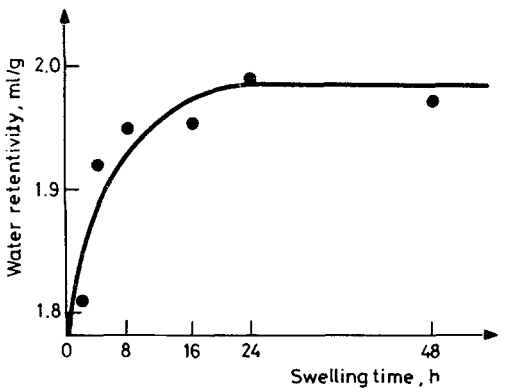

Fig. 2 Changes in water-retaining capacity of Crupodex^R as a function of swelling time

dried at 105° for 15 hours. The time-course of the swelling process for Crupodex^R is shown in Fig. 2.

Figure 2 shows that after 24 hours the swelling time has no further effect on the water-retaining capacity. Thus, it can be stated that the optimum swelling time for the two products is the same, and Crupodex^R and Debrisan^R take up water in an identical way.

The optimum drying time was determined by heating swollen and centrifuged Crupodex^R samples at a rate of 10 deg/min up to 105° and by keeping them at this temperature for 50–400 min (see Fig. 3).

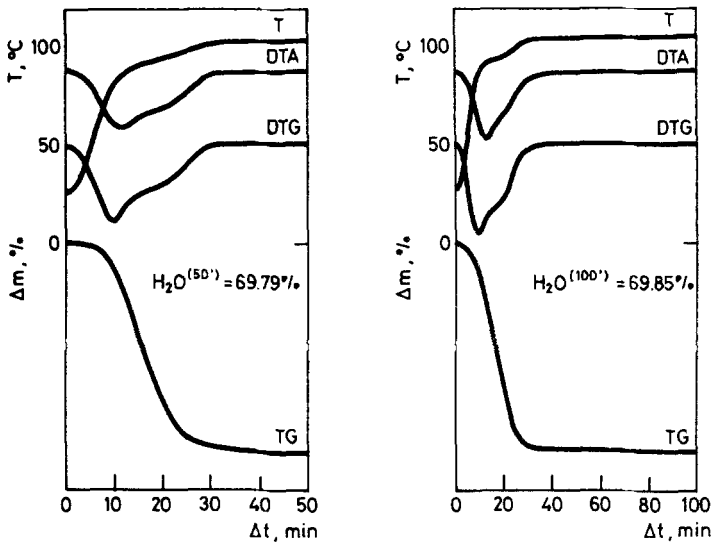

Fig. 3 Drying of swollen and centrifuged Crupodex^R at 105 °C for 50 or 100 min

It can be seen from Fig. 3 that Crupodex^R loses almost 99% of the absorbed water in 40 min at 105°. The loss of water is completed in 100 min. When the product is kept at 105° for a longer time (6–8 hours), a slight increase in weight is observed, which can presumably be explained by a surface oxidation process. After a fully dried sample has been left to stand in air at room temperature for 1–2 hours, the derivatographic curves show the strong water uptake by the product.

QMS–EGA investigation

Organic solvents such as ethanol, and to a lesser extent isopropanol, used in the manufacturing process for washing and drying, are retained in the final product. Determination of the upper limit of organic solvent content is very important with respect to the quality and usability of the product. The residual solvents can be determined on a gas chromatograph supplied with a head space analyser, but evolved gas analysis combined with mass-spectrometric detection (QMS–EGA) gives more complete information. The volatile components are identified on the basis of the complete mass-spectrum, while the changes in each component of given mass are monitored as a function of temperature with the aid of the peak selector. Removal of the water and ethanol content of an air-dried Crupodex^R sample is depicted as a function of temperature in Fig. 4. The water and the ethanol were measured via the peaks with mass numbers 18 and 45, respectively.

The water content of air-dried Crupodex^R dextranomer comes partly from the

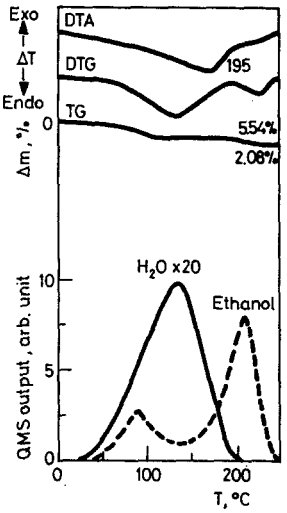

Fig. 4 Changes in water and ethanol contents of an air-dried Crupodex[R] sample as a function of temperature

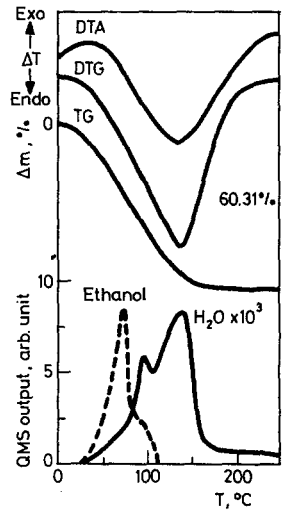

Fig. 5 Changes in water and ethanol contents of a water-swollen Crupodex[R] sample as a function of temperature

manufacturing process and partly from the adsorption of atmospheric moisture. The total amount is usually less than 10%. The loss of water begins at room temperature and is completed at 200°, with the highest rate at 140°.

Ethanol is evolved in two steps: a smaller maximum is observed at 95°, and a larger one at 210°. This suggests that ethanol is bound to the cross-linked dextranomer structure in two ways: in the intergranular spaces and inside the granules. Figure 5 shows the QMS–EGA spectrum of water and ethanol removal from a water-swollen Crupodex^R sample.

Water is evolved in two steps, first from the intergranular spaces and then, at higher temperature, from the interior of the granules. Ethanol, however, is removed in one step, with maximum rate at 70°. Accordingly, it can be stated that swelling in water causes ethanol to be displaced from the interior of the granules to the intergranular spaces. This phenomenon can be utilized in the solvent clearance of the dextranomer. The loss of isopropanol, which is always present, though in a much lower quantity than ethanol, takes place in a similar way.

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Zusammenfassung — Crupodex^R-Puder, ein vernetztes Dextranomer zum Trocknen und Säubern von Wunden, wurde mittels einiger thermoanalytischer Methoden untersucht. Zuerst wurden die TG, DTG und DTA Charakteristiken betrachtet und mit denen eines schon früher auf den markt gekommenen Produktes (Debrisan^R) verglichen. Die TG-Kurven wurden auch zur Untersuchung der Wasseraufnahme- und Trocknungsprozesse verwendet. Aus dem Produktionsprozeß verbliebene Lösungsmittelreste — hauptsächlich Ethanol — wurden mit einer Instrumentenanordnung Quadrupolmassenspektrometer-Derivatograph bestimmt. Mittels dieser Ergebnisse konnten einige Schlußfolgerungen betreffs des Mechanismus der Wasser- und Lösungsmittelaufnahme getroffen werden.

Резюме — Несколькими термоаналитическими методами был изучен декстраномер с поперечными связями (Краподекс), используемый в качестве высушивающего и очищающего

порошка. Проведенное исследование его методами ТГ, ДТГ и ДТА сопоставлено с другим продуктом, ранее обозначенным как Дебрисан. Кривые ТГ были также использованы при изучении сорбции воды и процесса высушивания. Следы органических растворителей, главным образом этанола, оставшиеся после процесса получения, были изучены с помощью квадрупольного масс-спектрометра, связанного с дериватографом. На основе полученных результатов сделаны некоторые заключения, касающиеся механизма сорбции воды и растворителей.