Effect of Drying and Cross-Linking on the Thermo-Analytical Characteristics of Gelatin

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Gelatin offers a variety of potential pharmaceutical uses. In the dry state it is used in capsule shells, but it could also serve as films for controlled release of active ingredients. It is sufficiently available and easy to handle. The fact, that gelatin dissolves in water at higher temperatures can be used for easy casting and results in an exact gel-point, but can also be disadvantageous for the in vivo use. However hardeners can be applied, that cross-link gelatin and make it completely insoluble. As an additional effect of this structural change, the cross-links densify the gelatin network, increase the resistance to scratches and make it less permeable. This should lead to reduced swelling in water and a lower diffusion coefficient for drugs.

The structural changes and their resulting characteristics of gelatin after heating or cross-linking are examined with different methods. Most commonly DSC and TGA are used [1, 2], but for swelling and water vapour uptake studies also the water vapour sorption test system SPS11 can be applied.

In DSC-studies increasing drying temperature for the gelatin solution proves to reduce irreversibly the enthalpy of fusion of gelatin films [3]. At a drying temperature above the melting temperature, no triple-helices are formed and the gelatin remains in the amorphous “hotform”, whereas at drying temperatures below 40°C more and more crystalline fractions (“coldform”) result, recognized by a higher enthalpy of fusion. Heating of the dry films shifts the thermo-analytical events to higher temperatures and breaks the triple-helices (no more enthalpy of fusion), but this process is reversible. With the use of a hardener the dissolution-peak of gelatin in water in the thermogram shifts to temperatures above 100°C, 128°C i.e., the melting and the glass transition temperature increase and the enthalpy decreases. This is due to the higher molecular weight of the protein chains and the loss of functional groups responsible for the formation of triple-helices. The water content of the films is reduced with increasing amount of hardener and the reduced swelling (from factor 10 for pure to factor 2 for cross-linked gelatin) starts at a higher relative humidity. This is measured with TGA and water vapour sorption (SPS-11). Sorption isotherms are produced, that are shifted to lower water uptake and higher relative humidity the more cross-linking agent is added.

[1] Reich, G., Pharm. Ind. 57, 1, 63-67 (1995)

[2] Fries, W., Lee, G., Biomaterials 17, 23, 2289-2294 (1996)

[3] Renner, M., Lippold, B. C., Proc. 4th World Meeting ADRITELF/APGI/APV, Florence, 8/11 April 2002, 1599-1600