

chondroitin sulfate films with 10%, 30% and 50% drug contents were prepared in the same manner.

The test on release of the drug from each product film was performed as follows. Thus, the test film was suspended in water (20° C.) or phosphate-buffered saline (PBS) (37° C.) and stirred. The liquid phase was sampled at predetermined intervals of time and its ultraviolet absorption spectrum at 269 nm was measured.

Table 10 shows the relationship of the water dissolution test data for the photocured hyaluronic acid films (DS= 0.7, 1.3, 1.8) having a drug content of 30% with DS and swelling capacity. As the dissolution test data, the time in which 20% of the drug was released from the film was used.

TABLE 10

DS	Swelling capacity	20% release time (min.)
0.7	8	25
1.3	5	120
1.8	0.2	360

It is apparent from Table 10 that, as a tendency, the higher the DS, the higher is the degree of crosslinking and, hence, the harder is the film, with a consequent decrease in swelling capacity and an associated decrease in the rate of release of the drug. This finding suggested that the water-absorbing capacity of a film is an important factor in the rate of drug release. Regarding the films with DS values of 1.3 and 1.8, the rate of drug release tended to decrease with an increasing drug content.

The photocured hyaluronic acid films (DS=0.7, 2.2) and photocured chondroitin sulfate films (DS=0.8, 1.3, 1.8) were compared for the rates of drug release in PBS at drug contents of 10% and 50%. The results are shown in FIGS. 26 through 30. It will be apparent from these graphs that the controlled release of the drug is feasible with films having DS values not less than certain thresholds (for CS-Thym, DS=1.3).

(2) Controlled release of heparin

In a 20% aqueous solution of DMF was dissolved the chondroitin sulfate-cinnamic acid ester [CS-Cin-4 (DS=1.37), CS-Cin-5 (DS=2.43)] obtained in Example 7 at a final concentration of 20% by weight as well as the hyaluronic acid-cinnamic acid ester [HA-Cin-3 (DS= 0.50), HA-Cin-5 (DS=1.28), HA-Cin-6 (DS=2.43)] obtained in Examples 1 and 2 at a final concentration of 10% by weight. To 10 ml each of these solutions was added 100 mg of heparin and the solution was coated on a glass sheet (10 cm×10 cm) and dried at room temperature for 1 hour to provide a film. This film was irradiated with a 450 W high-pressure mercury lamp for 30 minutes. The thickness of each film was approximately 100 μm.

Each of these films, as carried on the glass sheet, was completely submerged in a vessel containing 100 ml of water and stirred at 60 rpm. The amount of heparin released with time was determined by the carbazole-sulfuric acid method. The results showed that all the films provided for the controlled release of heparin.

Furthermore, each of the above controlled heparin releasing films was formed on the inner wall of a test tube. Then, in accordance with JP-A-4-41432, citrated blood was added and the clotting time was determined. All the samples showed antithrombotic activity.

(3) Controlled release of growth hormone releasing factor

In a 20% aqueous solution of DMF was dissolved the hyaluronic acid-cinnamic acid ester [HA-Cin-3 (DS= 0.50)]

at a final concentration of 10% by weight and 1 mg of growth hormone releasing factor (GRF, human; mol. wt. 5039.8) was mixed into 1 ml of the above solution. The mixture was then coated on a glass sheet (3 cm×3 cm) and dried at room temperature for 1 hour to provide a film. This film was irradiated with a 450 W high-pressure mercury vapor lamp for 30 minutes. The thickness of this film was 110 μm.

The above film as carried on the glass sheet was completely submerged in a vessel containing 10 ml of water and stirred at 60 rpm. The GRF released with time was assayed by high performance liquid chromatography and the cumulative amount of release was calculated. It was found that the controlled release of GRF could be successfully implemented.

EXAMPLE 29

Vascular Prosthesis

The inner surface of an artificial blood vessel with a small lumen (3 mm in inside diameter) was coated with a solution of the HA-Cin-3 obtained in Example 1 by the rotational coating technique and, after drying, the coated film cured with a UV irradiator utilizing a small caliber optical fiber, whereby a vascular prosthesis internally coated with cured hyaluronic acid was obtained.

EFFECTS OF THE INVENTION

The present invention can readily provide readily purifiable photocurable GAGs by selecting, as highly safe and biocompatible starting materials, those photoreactive compounds and glycosaminoglycans specifically mentioned herein and binding the former to the latter. The invention can further provide materials for medical use by irradiating said photocurable GAGs with light. The materials have a two- or three-dimensional network structure and are highly safe, biocompatible and biodegradable/absorbable. The invention can further provide crosslinked GAG-based materials having desired physical characteristics required of materials for medical use by appropriately selecting the molecular weight of GAG, the DS of photoreactive compound, and other factors. Thus the invention is very widely applicable in various field of medicine.

While the invention has been described in detail and with reference to specific examples thereof, it will be apparent to one skilled in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof.

What is claimed is:

1. A photocurable glycosaminoglycan derivative which comprises a glycosaminoglycan and a photoreactive compound covalently bonded to said glycosaminoglycan, wherein said glycosaminoglycan is at least one member selected from the group consisting of hyaluronic acid, chondroitin, chondroitin sulfate, dermatan sulfate, heparin, heparan sulfate, keratosulfate, keratopolysulfate and derivatives thereof, said photoreactive compound is at least one member selected from the group consisting of substituted or unsubstituted cinnamic acids and reactive derivatives thereof, uracil derivatives having a carboxyalkyl group as a substituent in position 1 and reactive derivatives thereof, and said photocurable glycosaminoglycan derivative is soluble in water and/or organic solvents and is curable by only irradiation with light.

2. A photocurable glycosaminoglycan derivative which