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ProductInformation

HEPARIN SODIUM
from Porcine Intestinal Mucosa
Sigma Prod. Nos. **H3393 and H9399**

CAS NUMBER: 9041-08-1
SYNONYMS: Heparinic acid (sodium salt)

PHYSICAL PROPERTIES:

Appearance: powder, white to off-white with faint yellow cast
Activity: Although from different suppliers, both products have minimum 140 U.S.P. units per mg solid (as is).[3]

STORAGE / STABILITY AS SUPPLIED:

Stored at room temperature, dry heparin is stable for years. It is reportedly stable for at least seven years, even at 30°C.[2]

SOLUBILITY / STABILITY OF SOLUTIONS:

Sigma tests sodium heparin at 50 mg/mL water. H3393 gives a clear solution, from colorless to faint yellow; H9399 gives a clear to very slightly hazy, colorless to faint yellow solution.[3]

Heparin is soluble in water up to 60% by mass, but essentially insoluble in methanol, ethanol or acetone.[2]

Solutions are stable in the pH range 4-9, and stable for years even at 37°C. No significant change in activity was seen in solutions autoclaved at 121°C for 5 to 10 minutes.[2] Prolonged autoclaving may not be recommended; sterilization should be done by filtration.[10]

BRIEF NOTES:

Heparin sodium is the salt of heparinic acid, which is unstable. A number of different salts are available, but the sodium salt is most commonly used as an anticoagulant. It may be dissolved in water, saline or buffer. It is reported to be incompatible with a number of common antibiotics.[10]

The U.S.P. unit is a measure of the anticoagulant properties of a given heparin product as it acts on antithrombin III (AT-III). Sigma does not perform a bioassay on heparin, but reports supplier data for each lot.

BRIEF NOTES: (continued)

The amount of heparin needed to prevent coagulation in whole blood lies between 20 units[11] and 50 units[12] per mL of whole blood. Since heparin is extemely soluble, a stock in normal saline may be prepared at a concentration convenient to the user, sterile-filtered and stored for use as needed.

More detailed information and references are provided below.

GENERAL REMARKS:

Heparin is a polymer classified as a mucopolysaccharide or a glycosoaminoglycan. It is biosynthesized and stored in mast cells of various mammalian tissues, particularly liver, lung and mucosa. Commercial heparin is chiefly isolated from beef lung or pork intestinal mucosa.[1]

Heparin has been used for years as an anticoagulant. Heparin binds to antithrombin III, a naturally occurring plasma protease inhibitor, accelerating significantly the rate at which antithrombin III (AT-III) inhibits coagulation proteases (factor Xa and thrombin).[4,5,6]

The activity of heparin as an anticoagulant has been shown to be related to the molecular weight; in the range of 6-12 kDa, heparin apparently binds to AT-III in a 1:1 stoichiometry. However, porcine heparin of MW 20 kDa can have two binding regions for AT-III, but the probability of a third region is negligible.[7,8] There is a correlation between molecular weight and anticoagulant activity, but it is linear only over a narrow range (8-12 kDa).[9]

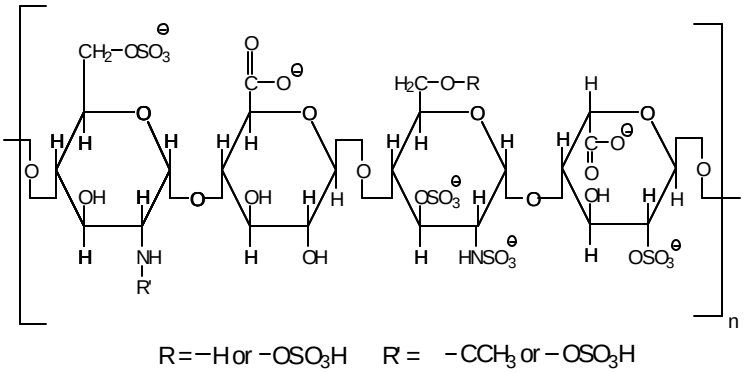
The action of heparin is clinically monitored using an activated partial thromboplastin time (APTT); these two products are not tested using APTT activity. Low molecular weight heparins (below approximately 8000 Da) inhibit AT-III but have a higher ratio of anti-factor Xa to anti-AT-III activity than regular heparin. They have lowered effect on platelet aggregation than normal heparin, and no significant effect on blood coagulation tests such as APTT. Dosages of these products cannot be equated to those of "normal molecular weight heparin".[10]

STRUCTURE:
Most of the structure of heparin can be accounted for by repeating disaccharide units consisting of 1,4-linked L-iduronic acid and D-glucosamine. The iduronic acid residues are O-sulfated at position 2, and the glucosamine residues are N-sulfated and O-sulfated at position 6. The repeating block can be interrupted or extended by residues of β-D-glucuronic acid and 6-O-sulfated N-acetyl-a-D-glucosamine.[1,2]

STRUCTURE: (continued)

Heparin A, isolated from porcine intestinal mucosa, differs from Heparin B, isolated from beef lung in that it has several times more "extender residues" compared to the latter type. See below for a structure.[1]

Heparin is a mixture of polyanion chains in a relatively wide range of molecular weights. Although it can range from as low as 6000 to as high as 30,000 Da[1], commercial heparins such as H3393 and H9399 have most chains in the range 17,000-19,000 Da.[3]



$R = -H$ or $-OSO_3H$ $\quad R' = -CCH_3$ or $-OSO_3H$

Heparin Partial Structure

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10. *Martindale: The Extra Pharmacopoeia*, 30th Ed. (Pharmaceutical Press, 1993), Reynolds, J.E.F., ed., 227-232.
11. Sigma Clinical Division, Technical Bulletin #870.
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