BioUpdate Foundation

HEPARIN NEWS UPDATE

Summer/Autumn 2011

Pharmacopeial changes for heparin monographs

Progress in the development of heparin analytical techniques is still being driven by the contamination incident of 2007-2008, in which some lots of unfractionated heparin were found to contain the semi-synthetic compound oversulfated chondroitin sulfate (OSCS). The USP, following the considerable 'Stage 2' revisions at the end of 2009 (http://www.usp.org/hottopics/heparin.html), is to add further assays to the heparin monographs in response to FDA requests. These are expected to go public next year, and will include ^{1}H NMR spectroscopy with higher sensitivity than at present, chromatographic identity with improved resolution and robustness, nucleotidic and protein impurities with tighter specifications than at present, a test for lipid content and a new molecular weight specification, supported by a method for determination of molecular weight distribution.

Concerns about the harmonization of heparin potency units

For the last 30 years or more, there has been a 7 – 13% disparity between the United States Pharmacopoeia (USP) unit and the International Unit (IU) for unfractionated heparin (http://www.ncbi.nlm.nih.gov/pubmed/11154108). It was therefore desirable to harmonize these two units for the measurement of heparin. The harmonization of the USP unit with the International Unit, however, caused more waves than anticipated. The FDA was concerned that this change in potency may have some clinical significance and a safety note was published on their website: (http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm184502.htm). A recent study in animals has also been published to show that this change in potency would probably have little impact on the safety and efficacy of unfractionated heparin in the US (http://www.ncbi.nlm.nih.gov/pubmed?term=Honchel%20heparin). It should be noted that in Europe unfractionated heparin products have always been labelled with IU and therefore, since 1973, European patients have been receiving "approximately 10%" less heparin than patients in the US, yet there have not been reports of "under dosage" in Europe.

Can bovine mucosal heparin be used to supplement the supply of porcine mucosal heparin?

The question of whether there really is a world shortage of heparin is a current source of controversy; rising prices of heparin have created the impression of a supply problem. Is the world so short of heparin that we have to look for other sources than porcine mucosa? The prospect of the re-introduction of bovine mucosal heparin to clinical use in Europe and the USA has been under much discussion recently. Both bovine and porcine mucosal heparins are used in other parts of the world. A paper from Paulo Mourao's lab (http://www.ncbi.nlm.nih.gov/pubmed/20216993) paints a worrying picture of bovine heparin with relatively low specific activity causing increased side effects (low specific activity means a higher dose in weight for the same dose in activity units implying an increased risk of side-effects). Is this a true species effect, or a result of suboptimal manufacturing processes? How does the structure of heparin vary with species? Not many papers are available on this subject so far, but the Brazilian labs have a strong tradition of exploring the variety of heparin structures between species.

Meetings news

There will be no heparin workshop in 2011, marking a break in the series of four meetings (organised jointly by NIBSC, the EDQM and the USP) in Potters Bar (2007), Strasbourg (2008), Rockville (2009) and London (2010). The 5th International Heparin Workshop will be held at the USP Headquarters in Rockville, Maryland on August 14-15, 2012. Enquiries should be sent to Dr Anita Szajek, at AEY@usp.org .

Upcoming BioUpdate Foundation course on Heparins

The next BioUpdate course on Heparins and Low Molecular Weight Heparins will be organised in Amersfoort, the Netherlands, November 19-20, 2012. This intensive post-experience course covers the structure and mechanisms of action of heparin and low molecular weight heparins, including the characterisation and standardisation of current heparin products, with special emphasis on newly introduced pharmacopoeial methods for identity, purity and potency of unfractionated heparin. Issues addressed above and the latest developments at the time of the course will also be incorporated in the course content.