^{111}In oxine thrombocytes

^{111}In-8-hydroxyquinoline

^{111}In oxine is used as an ingredient for the *in-vitro* radiolabelling of separated (autologous) blood cells which are subsequently administered intravenously for a variety of investigative purposes.

1. Indications

^{111}In-labelled platelets (thrombocytes): Determination of platelet survival and biodistribution, particularly spleen and liver uptake in cases of thrombocytopenia, arterial or vascular thrombosis, aneurysms and sites of inflammation in rejecting transplants. See chapter "Platelet kinetics".

2. Preparation

There are multiple methods described to label thrombocytes with ^{111}In oxine. The SmPC states:

- A volume of 42,5 ml of blood is collected in 7,5 ml ACD and centrifuged for 15 min at 200 g.
- The supernatant platelet rich plasma (PRP) is collected with a syringe and acidified with ACD, 0,1 ml per ml PRP. The PRP is centrifuged at 640 g.
- After removal of the supernatant platelet poor plasma (PPP), the pellet is resuspended in 3 ml sodium chloride (saline).
- Add 0,4 ml Tris buffer to 1 ml in oxinate. It is recommended to add the tris buffer just before the preparation is administered to the blood cells to prevent adsorption to the glass vial or syringe.
- Label the thrombocyte suspension with 4-37 MBq ^{111}In oxinate.
- Incubate at room temperature for 20 min.
- After incubation is completed, PPP is added to a volume of 5 ml and the radioactivity is measured.
- Free (unbound) Indium is removed (as supernatant) by centrifugation at 1000 g for 15 min.
- Thrombocytes are resuspended in 3 ml PPP.
- Additional PPP is added to a volume of 5 ml and radioactivity is measured again for the calculation of the labelling efficiency.
- The suspension is now ready for injection.

Special considerations:

- Working with blood can introduce risks to both the operator and the patient. The department labelling the cells should comply with all regulations. Adequate facilities, equipment, procedures and training for operators should be present. Additional the risks for blood contamination should be recognizes and precautionary measures should be implemented to minimise those risks.
- Platelet separation and labelling is easily confounded by the tendency for the

platelets to remain irreversibly aggregated in a pellet after centrifugation. Blood and subsequent platelet concentrate should not come in contact with glass or metal.

- ^{111}In oxine is a non-specific blood cell labelling agent and in the presence of whole blood it will rapidly form ^{111}In labelled transferrin. Therefore, care must be taken in the preparation of separated blood cells to be labelled to ensure separation of unwanted blood cells and other blood proteins.

3. Quality control

A variety of quality evaluations is possible. When developing a technique for labelling, use several methods.

Radiochemical purity

The labelling efficiency of the ^{111}In oxine labelled thrombocytes should be determined after labelling. The labelling efficiency is defined as the total radioactivity measured in the cells as a percentage of the total radioactivity measured in both the cells and the supernatant.

In general a labelling efficiency ≥80% is achieved, depending on the labelling technique.

Radionuclidic purity

Limit ≥99,75% as ^{111}In

Other quality controls

Several other quality control tests have been described.

Assessment of platelet harvest, assessment of platelet viability and function, in vitro aggregation studies, electron microscopy of the labelled cells to assess cellular shape changes and assessment of in vivo survival after injection are examples of tests that can be performed.

4. Interactions

No interaction studies have been performed.

5. Adverse reactions

Hypersensitivity (including fever, rash, urticaria, pruritus, anaphylactoid reaction).

6. Biodistribution & pharmacokinetics

Indium forms a saturated (1:3) complex with oxine (8-hydroxyquinoline). The complex is neutral and lipid-soluble, which enables it to penetrate the cell membrane. Within the cell, indium becomes firmly attached to cytoplasmic components; the liberated oxine is released by the cell. It is thought likely that the mechanism of labelling cells with ^{111}In oxine involves an exchange reaction between the oxine carrier and subcellular components which chelate indium more strongly than oxine.

Following intravenous injection of ^{111}In-labelled platelets in normal individuals some are rapidly taken up by the liver and spleen due to equilibration with the marginating cell pools in those organs. The residual cells remain in the circulation for a period determined by the remaining lifetime of the platelets.

Approximately 30% of the injected dose is immediately distributed in the spleen and about 10% in the liver. The remaining activity is cleared from the circulation with a half-life of about 4 days and is distributed in the spleen (5%), the liver (20%), the bone marrow (25%) and other tissues (10%). Normally, platelets survive in blood for about 9 days and are then destroyed on an age-dependent basis, mainly in spleen and bone marrow. Short survival times are associated with a variety of disease states such as thrombocytopenia. ^{111}In-labelled platelets will also accumulate at sites of active thrombus formation and imminent transplant rejection. Clearance of activity for labelled platelets from liver and spleen is very slow. In addition, there is very low excretion of activity in either urine or faeces. Elimination from the body is probably mainly through decay to stable cadmium, but for the purposes of radiation dosimetry calculations, body clearance is assumed to be analogous to that of ionic indium (half-life 70 days).

7. Stability

The SmPC does not mention a specific maximum shelf live. Once platelets are labeled with ^{111}In the label is stable at 37°C incubation for at least 4 h. It is essential that cells are viable when returned to the patient. In practice, longer periods of time between blood being taken from a patient and the cells being re-injected have provided no evidence of problems. However it is recommended to re-inject as soon as possible.

8. Literature

- SmPC Indium (In-^{111}) oxinate, radiopharmaceutical precursor; Mallinckrodt Medical; 2010.
- Bauman JM, Landry AJ. Practical platelet labeling with Indium-^{111}-Oxine. J of Nuc Med Tech 1986;14:15-7.
- AuBuchon JP et al. Platelet Radiolabeling Procedure. The Biochemical Excellence for Safer Transfusion (BEST) Collaborative. 2006.
- Goodwin DA et al. Indium-111-labeled autologous platelets for location of vascular thrombi in humans. J of Nucl med 1978;19:626-34.
- Thakur ML et al. Indium-111 labeled human platelets: improved method, efficacy and evaluation. J Nucl Med. 1981;22:381-5.
- Guidelines for the safe prepraration of radiolabelled blood cells. UK Radiopharmacy Group. 2009.