IMPLEMENTATION AND QUALITY CONTROL OF A 5% FRUCTOSE AND 10% GLYCEROL STERILE SOLUTION FOR DIGESTIVE ENDOSCOPY

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Abstracts

Background Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are innovative digestive endoscopic approaches allowing ‘en bloc’ tumour removal – which facilitates histological analysis and lowers the risks of local relapse. To ease complete tumour removal, both techniques require submucosal fluid injections. Nevertheless, no ready-to-use commercial solutions for submucosal injection are available.

Purpose To implement a simple production of a ready-to-use 5% fructose and 10% glycerol sterile solution (FGSS) for submucosal injection and appropriate quality controls.

Material and methods FGSS were aseptically compounded according to good manufacturing practices. Fructose and glycerol were mixed with isotonic sodium chloride in an ISO 5 controlled atmosphere area. The solution was sterile-filtered using rapid flow 0.22 µm filter units (ThermoScientific) and aseptically-filled into glass containers (125 mL) in a vertical laminar flow hood. An alternative method, using terminal sterilisation (121°C for 20 min), was also tested.

Quality controls were performed on three vials (beginning-middle-end of production). Fructose and glycerol concentrations were assessed by colorimetric-enzymatic methods adapted on a chemistry analyser (acceptance limits±10%). We developed a method of quantifying two fructose degradation products (5-hydroxymethylfurfural (SHMF) and 2-furaldehyde (2FA)) in FGSS, using a high-performance liquid chromatography UV Diode-Array-Detector. Accuracy profile serves for validation (relative acceptance limits±10%). Sterility assay and endotoxin testing (kinetic chromogenic method) were performed. Sub-visible particles contamination was assessed using a light-obscuration method (European pharmacopoeia (EP) 2.9.19 threshold: respectively 25 and 3 particles/mL for particles size ≥10 µm and ≥25 µm).

Results Our sterile-filtered compounding method allows the production of a sterile and bacterial-endotoxin-free FGSS. Particle load was 9.99 and 0.37 particles/ml respectively for ≥10 µm and ≥25 µm particles. Fructose and glycerol concentrations (g/L) were respectively at (mean (min-max)) 48.99 (47.04–50.39) and 127.39 (123.4–129.8)). Both SHMF and 2FA concentrations were below eu method’s limits of quantification (3.39 and 1.69 ng/mL respectively). When using the moist heat sterilisation method, the solution became light yellow and 5-HMF was 19.61 mg/L (far above EP specification).

Conclusion Our compounding method is simple, limits SHMF production and can be implemented in any hospital. Produced FGSS complies with the EP quality requirements. We developed the first specific and sensitive method for 5HMF and 2FA concentrations measurement in a FGSS preparation.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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