

CASE STUDY: DEVELOPMENT OF AN OINTMENT ACCORDING TO THE PHARMACEUTICAL INSPECTION CONVENTION GUIDELINE



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BACKGROUND AND IMPORTANCE

Haemorrhoids are pathology which affects to a significant community and hospital pharmacy burden. In non-severe cases, topical treatment is usually selected⁽¹⁾. In this ointment are combined the three pharmacological effects mainly found in commercial forms through a simple manufacturing procedure, accessible to the equipment and facilities of a hospital pharmacy laboratory.

The Pharmaceutical Inspection Convention⁽²⁾ published, in March 2014, a guideline to follow in Healthcare Establishments to ensure the quality of the medicines manufactured in the pharmaceutical services.

AIM AND OBJECTIVES

Prove the adequacy and suitability of the application of the current guidelines to the elaboration of medicines in hospital pharmacy; by means of an example intended to be easily transferred to other pharmacy departments.

Full development, as case study, of a semisolid pharmaceutical form, for haemorrhoids treatment containing a vasoconstrictor, a local anesthetic and a glucocorticoid⁽⁵⁾. As well as, the analytical procedures⁽⁷⁾ and the QA system to ensure its quality.

MATERIAL AND METHODS

Material: Ointment base: Vaseline, paraffin and levomenthol.

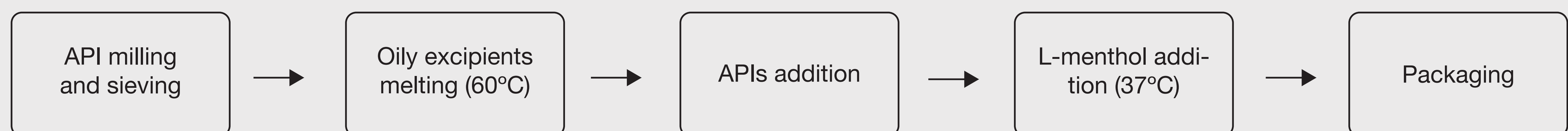
APIs (Active Pharmaceutical Ingredients): Phenylephrine Hydrochloride, Lidocaine Hydrochloride and Hydrocortisone.

Equipment: Electronic Analytical Balance Pinnacle; Chromatograph Agilent® Series 1100 with Quaternary Pump and Diode Array Detector; ThermoScientific® HAAKE Viscotester 550.

The organoleptic characteristics and rheologic properties were assessed. Content homogeneity proved through a HPLC validated method⁽³⁾.

RESULTS

COMPOUNDING



QUALITY CONTROL

- Study of the adequacy of the ingredients, materials, rooms, equipment and systems.
- Content uniformity assay (development and validation)⁽⁶⁾: Chromatographic method capable to determine the concentration of each API in the ointment (previous liquid:liquid extraction), and the purity of each API after milling.
- Rheological properties assay: Density, viscosity and extensibility.
- Definition of limits of acceptance for each property of the ointment.
- Sampling schemes for each of the assays.



QUALITY ASSURANCE

- Documental development and validation: Manufacturing guide (compounding), CoA (Certificate of Analysis) (final batches and raw, packaging and intermediate materials) QC (Quality Control), batch record document (compounding), standard operational procedures (compounding, QC and QA(Quality Assurance)).
- Internal audits.
- Raw, packaging material and final product approval.
- Development of CAPA system.
- Stability studies design.



CONCLUSION AND RELEVANCE

This work contributes to corroborate that the application of these guidelines in combination with International Conference of Harmonization instructions^(3,4) is both, feasible and convenient to manufacture medicinal products in healthcare establishments.

This methodology will be tried to implemented to more demanding medicinal products manufacture (such as tables and injectables) in subsequent and works.

REFERENCES

- (1) Brown SR. Haemorrhoids: an update on management. *Therapeutic advances in chronic disease* 2017 Oct; 8(10):141-147
- (2) Pharmaceutical Inspection Convenion. *Guide to Good Practices for the Preparation of Medical Products in Healthcare Establishments*. 2014
- (3) International Conference on Harmonization (ICH) of technical requirements for the registration of pharmaceuticals for human use. *Validation of analytical procedures: Text and Methodology Q2(R1)*. Geneva 2005
- (4) International Conference on Harmonization (ICH) of technical requirements for the registration of pharmaceuticals for human use. *Endorsed Guide for ICH Q8/Q9/Q10 Implementation*. Geneva 2011.
- (5) Rizkallal E, Machetti M, Pascual-Masiá L, Calvo MI, Martínez-Galán F (2019). *Pharmaceutical development of an ointment for hemorrhoids containing lidocaine, phenylephrine and hydrocortisone*. Poster. 39th Symposium de la AEFI. Barcelona (España)
- (6) Pascual-Masiá L, Machetti M, Rizkallal E, Calvo MI, Martínez-Galán F (2019). *Design and validation of a new HPLC method to quantify the three drugs of an ointment*. Oral communication. 39th Symposium de la AEFI. Barcelona (España)
- (7) Pascual-Masiá L. *Quality Control of the anti-hemorrhoidal ointment "Hemorrein"*. Master's Degree Thesis. September 29th. Pamplona (Spain)

