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Regulating innovation in compounded ophthalmic preparations

Regulación de la innovación en formulación magistral oftálmica

Ana Castro-Balado, Miguel González-Barcia

Pharmacy Department, Xerencia de Xestión Integrada de Santiago de Compostela (SERGAS), Santiago de Compostela. Spain. Clinical Pharmacology Group, Instituto Investigación Sanitaria Santiago Compostela (IDIS), Santiago de Compostela. Spain. Department of Pharmacology, Pharmacy and Pharmaceutical Technology. School of Pharmacy, Universidad de Santiago de Compostela, Santiago de Compostela. Spain.

Author of correspondence
Miguel González Barcia
Servicio de Farmacia Hospitalaria
Hospital Clínico Universitario
Calle A Chupana s/n.
15701 Santiago de Compostela, Spain.
Email:
miguel.gonzalez.barcia@sergas.es

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Since the 1980's, the development of compounded ophthalmic preparations by hospital pharmacy departments has carried on quietly, virtually unaffected, with topical formulations prepared from simple agents characterized by their limited ocular biopermanence and bothersome difficult-to-follow dosing schedules[1].

Personalized medicine, which tailors medical treatment to each patient's unique characteristics, is here to stay. Although, admittedly, the main protagonists of personalized medicine are pharmacogenetics and other omic sciences, compounding must definitely play an important role in its development. For that reason, it is essential to adapt the existing compounding units to current therapeutic demands, making sure they acquire the skills they need.

In the last few years, thanks to funding made available by the Spanish Foundation of Hospital Pharmacy (AISEFH 2013 and AISEFH 2019), there has been a resurgence of research projects dedicated to compounded ophthalmic preparations. In this respect, as mentioned in Castro-Balado *et al.*[2], compounding units have started to use a series of optimized easy-to-implement new vehicles such as hydrogels and contact lenses as drug-delivery systems. Although innovation, research and regulation are concepts that should go very much hand in hand in the hospital setting, the first two are often given precedence over regulatory considerations, giving rise to legal lacunae that may in one way or another delay the implementation of new developments.

Medical devices are currently subject to strict regulatory supervision, intended to ensure efficiency and patient safety. Both the European Commission and the Food and Drug Administration classify these products into three risk categories: low, medium and high. This classification also allows manufacturers to determine the need to carry out regulated clinical trials[3]. At present, there are a series of healthcare products whose chief goal is to facilitate application and/or administration of an active ingredient to its site of action. The Medical Devices Directive of the European Commission classifies these types of systems, which usually contain medicinal substances, under class III, which also includes endodontic materials with antibiotics, wound dressings with collagen or antimicrobial agents, condoms with spermicide and heparin-coated catheters, and other products. This area of medicine is currently booming as a result of the recent breakthroughs achieved in the development of new drug-releasing materials, which have resulted in the incorporation to clinical practice of revolutionary products like the drug-eluting stent.

Despite the above, the introduction of medical products into the field of compounding is a recent occurrence and is not yet covered by international regulations. Daily-wear soft and rigid gas-permeable contact lenses have been considered class II medical devices under the Medical Devices Directive since 1994, with only extended-wear lenses remaining under class III due to their higher risk of causing adverse events. Nowadays, they are commonly used as a therapeutic bandage in standard clinical practice following different ophthalmologic surgical procedures[4]. An emerging area of interest during the last decade was the use of contact lenses as drug-delivery systems to the cornea. Recent studies have shown their ability to carry, among others, certain anti-infectious drugs or cysteamine and promote the sustained release of their active component, preserving the blinking function and avoiding unproductive absorption of the drug[5]. However, the use of contact lenses as drug-delivery system poses regulatory concerns, specifically as to whether they should be classified as a medical device, a drug or a combination of both. If the medical device is only intended to deliver a drug, then if should be considered a drug. On the other hand, if it is a device with a certain indication (for example a non-erodible implant such as Vitrasert, approved for cytomegalovirus-associated retinitis, among others), it should be considered a combined product[6].

Fort the time being, none of these contact lenses has reached the market, although some severe ocular conditions, such as infectious keratitis, glaucoma or cystinosis, could benefit from their use. Patients requiring therapeutic contact lenses are bound to be able, in the short term, to benefit from a combined solution whereby the therapeutic drops will be instilled for the treatment of the patients' condition and the lenses will be used to promote epithelialization and healing.

Compounded preparations in this and other fields should constitute one more tool in the arsenal of personalized medicine, with new developments being grounded in new regulatory frameworks that provide due recognition and support to innovation in the realm of healthcare.

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