

Osmolality determination of poloxamer 407 thermosetting gels for ocular delivery

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Introduction: Poloxamer 407 is a poly(oxy ethylene)–poly(oxy propylene) block nonionic copolymer frequently used in pharmaceutical preparations due to its characteristic of thermoreversible gellification; therefore, it increases the product residence time. It is used in ophthalmic formulations and because the isotonicity is desirable for an ocular delivery system, the poloxamer's influence in the osmolality of the formulation must be evaluated. However, considering that concentrated solutions of the polymer are not easily frozen, it is difficult to analyze by freezing-point depression. Furthermore, one might suggest that as poloxamer is a large molecular weight nonionic molecule, the influence in the osmolality would be negligible. Therefore, poloxamer's influence in this colligative property was studied by direct measurement in osmometer and by the dilution method. **Objective:** Considering there is a lack of information about the influence of this polymer on the osmolality of solutions, the purpose of this study was to evaluate the influence of poloxamer 407 in the osmolality of a thermosetting gel for ocular delivery. Two different delivery systems were developed and one formulation was prepared to evaluate if the polymer wouldn't interfere in the osmolality of the product (NaCl was used to achieve the desired osmolality). Both delivery systems were evaluated by freezing-point depression in Osmometer, using two different methods. **Methods:** The formulations with desired gelation temperature were obtained using 20% of poloxamer 407 and 1% of chitosan (System A) and 18% poloxamer 407, 1% of chitosan and 41 mg of NaCl (System B). The samples were measured directly or were diluted with water and then measured in an osmometer. The dilution method was performed according to XV Japanese Pharmacopoeia and the osmolality was determined by calculation. A semi-micro osmometer K 7400 (Knauer, Germany) was used to analyze the samples. **Results:** System A presented an osmolality of 431.7 (± 11.9) mOsm/Kg and the same one evaluated by the dilution method showed a lower value (357.1 mOsm/Kg). System B presented 655.7 (± 2.9) mOsm/Kg and when evaluated by the dilution method showed a lower value (472.4 mOsm/Kg). A solution containing only 18% of poloxamer measured without dilution presented 399 (± 4.6) mOsm/Kg, so in this concentration the solution is already hypertonic. A solution of 41 mg NaCl and 1% chitosan showed desired value of osmolality (307.4 (± 2.5) mOsm/Kg). **Conclusion:** Poloxamer 407 influences the osmolality of a product and it must not be neglected during the development of a formulation. The direct measurement leads to more precise results, considering that the dilution method provided lower results, probably due to the error inherent to the dilution.

Keywords: Poloxamer 407, Osmolality, Ophthalmic delivery, Thermoreversible gel, Osmotic behavior

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