Formulation of indomethacin eye drops via complexation with cyclodextrins

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Abstract

PURPOSE:
Topically administered indomethacin is used in the management and prevention of ocular inflammation and cystoid macular edema related to cataract surgery and in the maintenance of mydriasis during cataract surgery. Pharmaceutically, the main obstacle in formulating indomethacin as eye drops is its low solubility and aqueous instability. Inclusion complexation of indomethacin with cyclodextrins (CDs) was our interest in this research to obtain stable and effective aqueous indomethacin eye drops.

MATERIALS AND METHODS:
The influence of β-CD, hydroxypropyl-β-CD (HP-β-CD), and sulfobutyl ether-β-CD (SBE-β-CD) on indomethacin solubility was investigated. Indomethacin-HP-β-CD complex was prepared and characterized by infrared spectroscopy, differential scanning calorimetry, and X-ray diffractometry and was subjected to in vitro release and stability studies. The anti-inflammatory effect of formulated indomethacin-HP-β-CD eye drops on chemically burned albino rabbit eyes was compared to those of Indocollyre(®) and Voltaren(®) eye drops.

RESULTS:
HP-β-CD was found to have a high solubilizing effect towards indomethacin and was thus selected for its formulation. Formulated indomethacin-HP-β-CD eye drops exhibited delayed release and high drug stability compared to the drug solution. Draize rabbit eye irritation test and histological examination on albino rabbit eyes treated with indomethacin-HP-β-CD eye drops revealed that these eye drops were non-irritant. The anti-inflammatory studies indicated that formulating indomethacin eye drops via complexation with HP-β-CD significantly improves the therapeutic efficacy of the indomethacin compared to the investigated eye drops.

CONCLUSION:
An aqueous ocular delivery system for the poor water soluble anti-inflammatory indomethacin was prepared using HP-β-CD as a complexing agent. Besides a sufficient solubility for the drug, many factors were studied in the development of this system, such as stability and safety. In addition, indomethacin-HP-β-CD eye drops showed promising management to corneal inflammation.

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