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Drug release from membranes of hyaluronic acid and its esters

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Drug release from three types of hyaluronate based (sodium hyaluronate and ethyl and benzyl esters of hyaluronic acid) membranes was investigated. In the membranes, drug was either: 1) physically incorporated, 2) physically incorporated in the membrane, then laminated with a second polymer or 3) covalently bound to the polymer. The release of model compounds was found to be rapid when the compounds were physically incorporated; the release could be slowed by laminating the core membranes. Permeability and partition coefficient values were used to explain the release profiles. The amount of drug released was linearly related to the square root of time for both "physically incorporated" and "laminated" systems. When drug was covalently bound to the polymer, the release was slow and near zero-order. The solubility of the polymer and/or the hydrolysis of ester bonds are thought to be some of the important processes involved in drug release. The results suggest that a range of release rates can be achieved with hyaluronate based membrane systems.

Key words: Esters of hyaluronic acid; Glycosaminoglycans; Polymeric prodrugs; Permeability coefficient

Introduction

Hyaluronic acid (HA) is an endogenous glycosaminoglycan found in various tissues, including connective tissue, the synovial fluid of joints and the aqueous humor of the eye [1]. This report presents various procedures for preparing drug-loaded membranes of esters of HA and the resulting in vitro release profiles. Model compounds were either physically incorporated in the membranes or covalently bound to HA through ester linkages. These model compounds were selected based on their charge and on their applicability for dosage forms. Among these, hydrocortisone and benzyl alcohol are neutral, mafenide acetate is positively charged, and fluorescein sodium and hydrocortisone hemisuccinate are negatively charged at neutral pH. These model compounds are currently used as active agents in dosage forms (hydrocortisone, hydrocortisone hemisuccinate, and mafenide acetate) [2], as a pharmaceutical aid (benzyl alcohol) [3] and as a diagnostic aid (fluorescein sodium) [4].

An objective of this project is to ascertain whether the membrane drug release profiles can be explained using physical constants. The permeabilities and partition coefficients for these compounds in ethyl, benzyl and partial benzyl ester membranes of HA have been studied. Many previous articles have reported transport properties of membrane systems [5–7] and using the data, the release profiles often can be predicted.

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