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Mini-Review

Topical therapies for skin cancer and actinic keratosis

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This paper is dedicated to the cherished memory of Tafida, daughter of Tasnuva Haque.

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ABSTRACT

The global incidence of skin cancer and actinic keratosis (AK) has increased dramatically in recent years. Although many tumours are treated with surgery or radiotherapy topical therapy has a place in the management of certain superficial skin neoplasms and AK. This review considers skin physiology, non-melanoma skin cancer (NMSC), the relationship between AK and skin cancer and drugs administered topically for these conditions. The dermal preparations for management of NMSC and AK are discussed in detail. Notably few studies have examined drug disposition in cancerous skin or in AK. Finally, recent novel approaches for targeting of drugs to skin neoplasms and AK are discussed.

Contents

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1. Introduction

Skin cancer is the most common cancer in Caucasian populations (Byrd-Miles et al., 2007). Damage of skin cell deoxyribonucleic acid (DNA) by ultraviolet (UV) radiation followed by failure of DNA repair mechanisms is the primary cause of these neoplasms. In the early stages, skin cancers develop in the outer layers of the skin. If not treated, they may grow deeper into the skin with development of metastases (secondary malignant growths distant from the primary origin). An actinic keratosis (AK) or solar keratosis is a scaly or crusty growth on the skin indicative of sustained damage by the sun. AK may progress to invasive neoplasms and has been interpreted as the earliest sign of skin cancer (Ibrahim and Brown, 2009). Early diagnosis is critical for the effective prognosis and treatment of patients with skin cancer. However, anticancer drugs which are administered orally or by the intravenous route are associated with serious side effects especially when given systemically. Topical dosage forms deliver most of the drug locally with fewer side effects compared with other routes of administration.

To date, a very limited number of molecules has been administered topically to skin cancer lesions or AK. This article provides a brief overview of skin physiology, describes the location and classes of skin cancers amenable to topical therapy and outlines the AK – skin cancer continuum. Surgery and chemotherapy are the definitive treatments for melanoma; therefore this type of cancer is only briefly reviewed here (Maverakis et al., 2015). Topical formulations are examined and, where available, skin penetration properties of the various drugs are detailed. New strategies for targeted drug delivery to skin cancers and AK are considered with an emphasis on studies conducted *in vitro* with porcine or human tissue, or in patients.

2. Skin structure and physiology

The various skin layers, appendages and cell subtypes are presented in this section as a prelude to discussion of the skin cancers most commonly reported, their causalities and location in the skin, which is detailed in the following section.

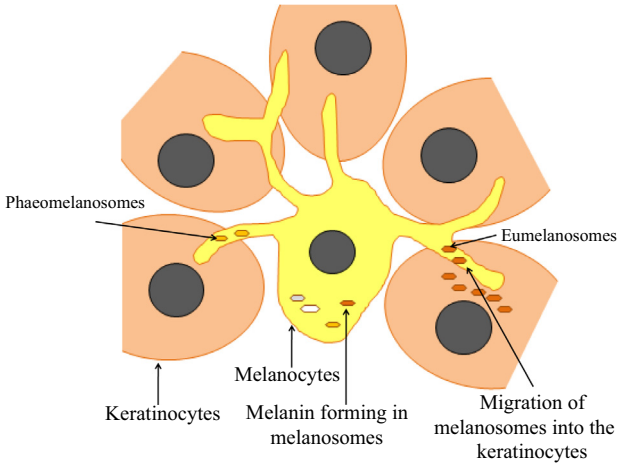

Fig. 2. Melanocytes and migration of melanosomes through the dendritic extensions to the surrounding keratinocytes (adapted from Wood and Bladon, 1985).

2.1. Epidermis

The skin acts as an interface between the internal organs and the environment. It is the largest organ of the human body and accounts for 10% of anatomic weight. Structurally, the skin is a multi-lamellar organ and it is involved in several physiological functions. The three layers of the skin are the epidermis, dermis and subcutaneous tissue. The outermost lamina of the epidermis, the stratum corneum (SC) represents the major barrier. This unique membrane prevents excessive water loss and is the major route for the percutaneous absorption of exogenous material as reviewed in detail by Menon et al. (2012), and Baroni et al. (2012).

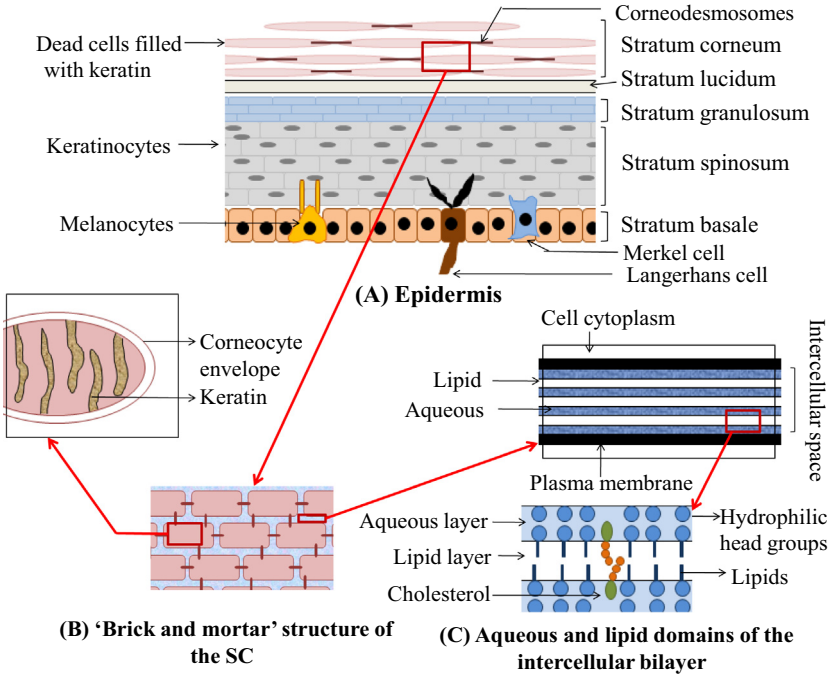

Fig. 1. Diagrammatic representation of: (A) layers of human epidermis, (B) 'brick and mortar' organisation of the SC, and (C) organisation of aqueous and lipid domains in the intercellular bilayer region.