

CHAPTER 1

Introduction

The present pharmaceutical products are available in several forms which are the oral solid, liquid and semisolid preparations. To attain the therapeutic efficiency of those preparations, the application depends on the suitability of pharmaceutical regulation and dosage form. Cream and lotion are the popular topical products, besides, the patch used for local or transdermal delivery system is an alternative application. The local effect of the patch is performed directly in the skin and may provide more convenient application than conventional one (oral, parenteral and topical use). Discharging a patch out of the skin surface can terminate the therapeutic effect, whereas systemic overdose from oral and parenteral routes may be observed (1). Therefore, the patch application is more feasible for preventing any unexpected effect than those of conventional routes.

One of skin disorders frequently disturbing affected patients is the hyperpigmentation so-called melasma. It is generated from melanocytes erroneous leads to an unusual increase of melanins inside the skin particularly at the light exposed areas such as face and arms, and the darker skin often appears in long term. However, there is still no excellent treatment to vanish the hyperpigments permanently from the skin. The possible approaches for melasma elimination are minimizing the hyperpigments associated with prevention of their recurrent by avoiding strong light and sun-blocked application. There are melasma depleting agents such as bismuth subgallate, bismuth subnitrate, hydroquinone, ammoniated mercury, azelaic acid and monobenzone (45). An interesting agent for hyperpigmentation treatment is tranexamic acid. It has been classified as an antifibrinolytic agent used to prevent and treatment for bleeding disorder caused by decomposition of fibrins (2). Some report studied by Maeda and Naganuma (3) demonstrated the preventive activity of tranexamic acid in pigment disorders. For its freely solubility in water, tranexamic acid is able to be prepared in many dosage forms for oral, parenteral and topical routes. Moreover, it is possible to produce in patch preparation in order to

deliver the active ingredient into the skin at the target area. The aqueous miscible property of tranexamic acid allows it to be formulated with hydrogel system. Thus, the patch of tranexamic acid in hydrogel matrix has been studied. The gel preparation has most of aqueous in its component, and requires thickening or/and gelling agents known as polymers, for example; agar, alginic acid, cellulose and its derivatives including carbopol (46). These polymers are generally miscible to water, some has poor solubility but is able to swell in an aqueous system. The amount and category of polymer mainly regulate the viscosity of gel formulation. The gel consists of approximately 60-90% w/w of water and three-dimensional networks of hydrophilic polymer, so-called hydrogel (4), performs a special property such that it can easily swell in wet condition as well as shrink in dehydrated condition. However, this behavior depends on its nature and density of networks. Several applications of hydrogel have been established such as flexible soft contact lens that can be sterilized by autoclave including a topical hydrogel for wound dressing proved for its non antigenic property.

The hydrogel patch of tranexamic acid has been developed to achieve an appropriate formulation used for local effect on the skin. The patch should provide good stability, physical properties (adhesion, optimal pH, texture, flexibility, non-allergy, etc.) as well as appropriate drug release. In order to obtain the release profiles of tranexamic acid from the patches, it requires a special method that is the derivatization with a selective reagent. Naphthalene-2,3-dicarboxaldehyde (NDA), a selective fluorogenic reagent for primary amines, is possibly used to react with tranexamic acid for the spectrofluorometric analysis. This convenient method was developed and validated in this study for determination of tranexamic acid formulated in a patch preparation. Furthermore, this study proposes the alternative preparation and application of tranexamic acid, that will probably be beneficial to dermatological research and the treatment of melasma.