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Review

Thin films as an emerging platform for drug delivery

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ABSTRACT

Pharmaceutical scientists throughout the world are trying to explore thin films as a novel drug delivery tool. Thin films have been identified as an alternative approach to conventional dosage forms. The thin films are considered to be convenient to swallow, self-administrable, and fast dissolving dosage form, all of which make it as a versatile platform for drug delivery. This delivery system has been used for both systemic and local action *via* several routes such as oral, buccal, sublingual, ocular, and transdermal routes. The design of efficient thin films requires a comprehensive knowledge of the pharmacological and pharmaceutical properties of drugs and polymers along with an appropriate selection of manufacturing processes. Therefore, the aim of this review is to provide an overview of the critical factors affecting the formulation of thin films, including the physico-chemical properties of polymers and drugs, anatomical and physiological constraints, as well as the characterization methods and quality specifications to circumvent the difficulties associated with formulation design. It also highlights the recent trends and perspectives to develop thin film products by various companies.

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1. Introduction

Generally, thin films can be referred as a thin and flexible layer of polymer with or without a plasticizer [1]. Since they are thin and flexible by their nature, it can be perceived to be less obtrusive and more acceptable by the patient [2]. The thin film is polymeric matrices that meet many requirements for being used efficiently as a drug release platform [3]. Fundamentally, thin films are excellent candidates for targeting sensitive site that may not be possible with tablets or liquid formulations [4]. Thin films have shown the capabilities to improve the onset of drug action, reduce the dose frequency and enhance the drug efficacy [3]. Similarly, thin films may be useful for eliminating side effects of a drug and reducing extensive metabolism caused by proteolytic enzymes [5,6]. Ideal thin films need to exhibit desirable features such as sufficient drug loading capacity, fast dissolution rate or long residence time at the site of administration, and acceptable formulation stability. They should also be non-toxic, biocompatible and biodegradable [7,8].

Compared with the existing traditional dosage forms, it stands out to be superior in terms of enhanced bioavailability, high patient compliance, and patent extension of active pharmaceutical ingredients (API) [9]. Furthermore, thin film formulations offer several advantages, including (a) convenient administration through non-invasive routes, (b) ease of handling during manufacture and transportation, and (c) cost-effectiveness in the development of formulations [8,10,11]. The availability of a wide array of suitable polymers and the paradigm shift in manufacturing technology have made possible to develop a wide range of thin films [12]. Therefore, a thin film is gaining popularity and acceptance in the pharmaceutical arena as a novel drug delivery dosage form.

Substantial efforts have been made to formulate polymeric thin films that are administered generally *via* buccal, sublingual, ocular and skin routes [13,14]. Among different routes, the use of thin films for delivering medicine into sublingual or buccal mucosa has drawn immense interest in recent years [15]. Meanwhile, ophthalmic films are currently developed for overcoming the ocular barriers and preventing loss of drugs through the lacrimal drainage system [16]. Controlling compositions of polymers of different grades has facilitated the modification of key characteristics of thin films such as drug release rate, mucoadhesive properties, mechanical strength and other related properties. Additionally, various inactive components can be included such as fillers, plasticizer, saliva stimulating agent, colorants, and sweeteners for improving aesthetic characteristics. Many pharmaceutical companies are fascinated by the appealing features of thin films, and as a result they have already patented various technologies for producing thin films [17].

Currently, a significant amount of original works and patents can be found in literature, but still there is a need for extensive studies to optimize the performance of thin films accurately. The lack of appropriate guidance for the manufacture, characterization and quality control of the thin films has sought the need of adequate studies in this area from the pharmaceutical viewpoint. Therefore, this paper will contribute to give insights on understanding the critical quality attributes and characterization methods with the aim to enhance the performance of thin films.

2. Types of thin films

Thin film is not a recent formulation, and it was first introduced in late 1970 to overcome swallowing difficulties exhibited by tablets and capsules [15]. Various names of thin films appeared, such as oral film (oral thin film), oral soluble film, wafer, oral strip, orodispersible film (ODF), buccal film, mucoadhesive film, ophthalmic film, and transmucosal film. While several films are designed to be dissolved quickly in the oral cavity for the absorption of a drug in the gastrointestinal cavity (oral and oral soluble, or orodispersible films), some are prepared to deliver a drug at the site of administration (e.g., buccal, sublingual and ophthalmic thin films). Drugs with high mucosal permeability have been known to be suitable for buccal and sublingual delivery with films [18]. Likewise, ophthalmic thin films are generally applied to treat diseases of the anterior segment such as conjunctivitis, glaucoma and chronic dry eye syndromes [5,19].

A film that readily dissolves in the oral cavity is generally termed as orodispersible film according to European Medicines Agency (EMA) or simply soluble film according to FDA [3]. Usually, fast dissolving oral films are ultra-thin film (50–150 μm) having size of postage stamp, which dissolves within a minute in the oral cavity after being in contact with the saliva, resulting in quick absorption and instant bioavailability of the drugs [20,21]. Drugs loaded in buccal adhesive films are absorbed directly *via* buccal mucosa, which delivers the drug to the systemic circulation after their absorption [22]. Likewise, wafer is frequently mentioned as paper-thin polymeric films employed as carriers for pharmaceutical agents. This innovative dosage form is taken orally but does not require water to swallow for the absorption of a drug [23]. Orodispersible films should not be misunderstood with buccal films designed for staying longer on the cheek mucosa [24]. Therefore, different types of films should be distinguished accurately to prevent possible misinterpretations.

3. Advantages of thin films as an emerging dosage form

3.1. *Advantages over conventional dosage forms*

A thin film dissolves rapidly than other conventional dosage forms [25]. Thin films are less friable and easy to carry dosage form compared to commercialized orally fast disintegrating tablets, which need special packing. Likewise, a single dose of strip can be carried individually without requiring the secondary container [26,27]. It is very important to address the poor stability of liquid dosage forms, especially the aqueous formulations. Unlike the thin films, there is a need for great care during accurate measurement of the amount and shaking the bottle every time before administration may contribute to less acceptance by the patients [3]. Conventional ophthalmic drug delivery systems such as eye drops or solutions are commonly used but they are limited in their ability to provide high ocular drug bioavailability and sustained duration of action [28]. Ophthalmic thin films can be used to improve the drug delivery to the eye. In contrast to transdermal patch, the transdermal film is less associated with skin irritation due to less