International Journal of Pharmaceutics 481 (2015) 18–26

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Double layer adhesive silicone dressing as a potential dermal drug delivery film in scar treatment

Krystyna Mojsiewicz-Pieńkowska [a,*], Marzena Jamrógiewicz [a], Maria Żebrowska [b], Barbara Mikolaszek [b], Małgorzata Sznitowska [b]

[a] Department of Physical Chemistry, Faculty of Pharmacy with Subfaculty of Laboratory Medicine, Medical University of Gdansk, 80-416 Gdańsk, Al. Gen. Hallera 107, Poland

[b] Department of Pharmaceutical Technology, Faculty of Pharmacy with Subfaculty of Laboratory Medicine, Medical University of Gdansk, 80-416 Gdańsk, Al. Gen. Hallera 107, Poland

ARTICLE INFO

Article history:
Received 4 December 2014
Received in revised form 24 January 2015
Accepted 28 January 2015
Available online 29 January 2015

Keywords:
Skin dressing
Adhesion
Occlusion
Hydration
Oxygen and water permeation

ABSTRACT

The present studies focused on the evaluation of design of an adhesive silicone film intended for scar treatment. Developed silicone double layer film was examined in terms of its future relevance to therapy and applicability on the human skin considering properties which included *in vitro* permeability of water vapor and oxygen. In order to adapt the patches for medical use in the future there were tested such properties as *in vitro* adhesion and occlusion related to *in vivo* hydration. From the silicone rubbers double layer silicone film was prepared: a non-adhesive elastomer as a drug carrier (the matrix for active substances – enoxaparin sodium – low molecular weight heparin) and an adhesive elastomer, applied on the surface of the matrix. The novel adhesive silicone film was found to possess optimal properties in comparison to commercially available silicone dressing: adhesion *in vivo*, adhesion *in vitro* – 11.79 N, occlusion $F = 85\%$ and water vapor permeability *in vitro* – WVP = 105 g/m^2/24 h, hydration of stratum corneum *in vivo* $H = 61–89$ (RSD = 1.6–0.9%), oxygen permeation *in vitro* – 119–391 cm^3/m^2/24 (RSD = 0.17%). *In vitro* release studies indicated sufficient LMWH release rate from silicone matrix. Developed novel adhesive silicone films were considered an effective treatment of scars and keloids and a potential drug carrier able to improve the effectiveness of therapy.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Among polymers commonly indicated for medical purposes, silicones are considered as materials possessing unique properties, described in detail by other authors in the publications (Boateng et al., 2008; Snorradóttir et al., 2011; Schroeder et al., 2007; Valenta and Auner, 2004; Rajendra et al., 2010; Mojsiewicz-Pieńkowska et al., 2011). Among silicone-based materials designed for skin application, where proper attachment onto the skin is essential for therapy effectiveness, most common are: pressure-sensitive silicone adhesives (PSSA), used in the formulation of transdermal patches (Ho and Dodou, 2007; Rippon et al., 2007), silicone soft skin adhesives (SSA), used in advanced wound care treatment as matrices for delivery of active substances (Rippon et al., 2007; Moris et al., 2009), modern dressings used in therapy of chronic wounds (so called active dressings) (Valenta and Auner, 2004), soft silicone dressings, used for prevention of scarring in an acute traumatic wound (Meuleneire, 2007), silicone gel dressings (De Oliveira et al., 2001), silicone gel sheetings (SGS) (Borgognoni, 2002) and silicone-filled cushions (Berman and Flores, 1999) used for surgical scars. Unique application of silicone elastomers related to their physical properties is scar therapy, mostly therapy of hypertrophic scars, keloids and burn scars (Berman et al., 2007; Momeni et al., 2009; Bloemen et al., 2009; Mustoe, 2008; Van den Kerckhove et al., 2001; Wolfram et al., 2009). Exact mechanism of silicones effectiveness in scar therapy is still unknown, but these preparations are commonly applied as a standard procedure. In the modern medicine, scars still present a very serious problem, not only because of aesthetic reasons, but also due to health issues (contractions, pruritus, inflammation). The treatment of scars is time-consuming, often ineffective, sometimes painful, and for these reasons it was covered by an international program. In 2002 the guidelines for clinical recommendations were published by an international advisory panel on scar management, based on a qualitative overview of 300 references as well as on expert consensus on best practices (Gauglitz et al., 2011; Mustoe et al., 2002). The usage of silicone gel sheeting was considered as a simple, safe and effective method of prophylaxis, which prevents

* Corresponding author. Tel.: +48 58 349 16 56; fax: +48 58 349 16 51.
E-mail address: kpienk@gumed.edu.pl (K. Mojsiewicz-Pieńkowska).

http://dx.doi.org/10.1016/j.ijpharm.2015.01.050
0378-5173/© 2015 Elsevier B.V. All rights reserved.

formation of scars and keloids. In case of therapy of the majority of existing scars, the usage of SGS is recommended as a first-line therapy.

In the current paper *in vitro* characteristics of occlusive properties and permeation of water vapor and oxygen, as well as results of *in vivo* determination of skin hydration and adhesion, for novel silicone based patch are presented. According to the present state of knowledge, these properties may influence the "repair" mechanism of not only "fresh" scars and keloids but also of mature scars existing for several years (Momeni et al., 2009; Bloemen et al., 2009; Mustoe, 2008; Van den Kerckhove et al., 2001; Wolfram et al., 2009; Gauglitz et al., 2011). Limited number of publications, presenting in details results obtained for silicone films applied on the skin and evaluating their physical and chemical properties in terms of skin applicability, can be found. Material characteristics may be beneficial in enabling future recognition of complicated mechanism of therapeutic action of silicone materials on scars and keloids (Table 1). In order to estimate probability of developed film effectiveness in both skin applicability and scar treatment, comparative analysis with commercial self-adhesive silicone gel sheet, with well-recognized therapeutic efficacy (Cica-Care) was conducted. As to extend the applicability of DLASil (double layer adhesive silicone film) in scar treatment, low molecular weight heparin (LMWH) was incorporated in silicone matrix. Enoxaparin sodium (LMWH) was chosen as a model drug requiring long-term application which determines therapeutic effectiveness. Previous *in vivo* and *in vitro* research showed the efficacy of heparin commonly used in topical preparations such as gels and ointments for treatment of hypertrophic scars and keloids due to influencing human skin fibroblast cells (Karagoz et al., 2009; Pikuła et al., 2014). Silicone films containing enoxaparin (LMWH) were developed as an alternative for inconvenient daily application of silicone dressing without active substances. Silicone sheets can be applied on the skin for several days, which minimizes risk of therapy abandonment. However, effectiveness of such preparations is strongly affected by release of sufficient amount of active ingredient, which was also evaluated in *in vitro* experiment.

2. Materials and method

2.1. Materials

Two-part silicone rubber Gumosil AD-1 (parts A and B) and silicone oil Silol (viscosity 350 cStIt is correct.) were obtained from Silikony Polskie (Nowa Sarzyna, Poland). Two-part adhesive silicone rubber soft skin adhesives MG7-9850 (parts A and B) was obtained from Dow Corning (Wiesbaden, Germany). Commercially available silicone sheeting Cica-Care (Smith and Nephew, Hull, UK) (Fabo, 1996) was used for comparative purposes. Enoxaparin sodium salt (LMWH, low-molecular-weight heparin) was obtained from Welding (Hamburg, Germany). Isopropyl myristate (MIP) was purchased from Sigma–Aldrich (St. Louis, MO, USA).

2.2. The preparation of the adhesive silicone film

Double-layer adhesive silicone film (DLASil) was prepared, composed of the following layers (Fig. S1):

1. Gumosil AD-1 non-adhesive silicone elastomer layer, potential matrix for active substance; thickness 0.35 cm,
2. adhesive silicone elastomer layer (soft skin adhesive, Dow Corning, DC 7-9850), which assures constant contact between non-adhesive layer and the skin, thickness 0.15 cm.

Supplementary material related to this article found, in the online version, at http://dx.doi.org/10.1016/j.ijpharm.2015.01.050.

Microscopic imagining was used to measure thickness of each layer.

Firstly, non-adhesive layer was obtained by mixing two components Gumosil AD-1 part A with part B) in 10:1 (w/w) ratio, and the prepared mixture was casted on the surface with

Table 1
The influence of silicone elastomers properties on mechanism of therapeutic action on scars and keloids.

Property	The action on skin and the mechanism of therapy	References	Comment
Adhesion to the skin	- provides optimal occlusion which contributes to the hydration of stratum corneum	(Rippon et al., 2007; Wokovich et al., 2006)	Enables the application, guarantees the occlusion as well as hydration of stratum corneum, and therefore, influences effective transport of active substances to the skin
Occlusion of the skin and limited permeation of water vapor	- causes hydration of *epidermis* and therefore creates the proper conditions for standard maturation of a scar; - while the compression of the skin causes the optimization of pressure, which may influence the reduction of fibroblasts as well as collagen disintegration; - enhances the efficacy of scar treatment; - stimulates angiogenesis which causes the creation of new capillaries	(Schroeder et al., 2007; Berman and Flores, 1999; Berman et al., 2007; Wolfram et al., 2009; Pikuła et al., 2014; Jungersted et al., 2010; Gold et al., 2001; Stavrou et al., 2010; Tandara and Mustoe, 2008; Gallant-Behm and Mustoe, 2010; Kloeters et al., 2007; Gilman, 2003a,b)	Increases the hydration of stratum corneum which enables the permeation of active substances to the skin. The limited permeation of water vapor prevents drying and apoptosis of epidermal cells and enhances epidermal migration
Hydration of stratum corneum	- inhibits either of fibroblasts proliferation or collagen synthesis occurs; - softens the epidermis which decreases undesired symptoms (pain, pruritus, contraction)	(Wolfram et al., 2009; Suetake et al., 2000; Sawada and Sone, 1992)	Enables the permeation of active substances and stimulation of many processes which provide homeostasis
Oxygen permeation	- stimulates the process of epithelialization; - results in healing of epidermal barrier defects as well as in repair process of keloid tissue; - positively influences on fibroblasts which produce collagen; - stimulates the process of angiogenesis	(Tandara and Mustoe, 2008; Gallant-Behm and Mustoe, 2010; Gilman, 2003a; Kurian et al., 2003; Prado et al, 2008)	Oxygen exerts antibacterial activity due to the formation of neutrophils. This prevents the formation of pathological microbiological environment under the patch during prolonged wearing. High permeation of oxygen and other gases prevents the formation of partial pressure in skin under the patch

Download English Version:

https://daneshyari.com/en/article/2501514

Download Persian Version:

https://daneshyari.com/article/2501514

Daneshyari.com