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Influence of hydrophilic polymers on functional properties and wound healing efficacy of hydrocolloid based wound dressings

Sung Giu Jin[a,1], Abid Mehmood Yousaf[a,b,1], Kyeong Soo Kim[a], Dong Wuk Kim[a], Dong Shik Kim[a], Jin Ki Kim[a], Chul Soon Yong[c], Yu Seok Youn[d], Jong Oh Kim[c,**], Han-Gon Choi[a,*]

[a] College of Pharmacy & Institute of Pharmaceutical Science and Technology, Hanyang University, 55 Hanyangdaehak-ro, Sangnok-gu, Ansan 426-791, South Korea
[b] Faculty of Pharmacy, University of Central Punjab, 1-Khayaban-e-Jinnah, Johar, Lahore 54000, Pakistan
[c] College of Pharmacy, Yeungnam University, 214-1, Dae-Dong, Gyongsan 712-749, South Korea
[d] School of Pharmacy, Sungkyunkwan University, 300 Cheoncheon-dong, Jangan-gu, Suwon 440-746, South Korea

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ABSTRACT

The purpose of this study was to investigate the influence of different hydrophilic polymers on the swelling, bioadhesion and mechanical strength of hydrocolloid wound dressings (HCDs) in order to provide an appropriate composition for a hydrocolloid wound dressing system. In this study, the HCDs were prepared with styrene-isoprene-styrene copolymer (SIS) and polyisobutylene (PIB) as the base using a hot melting method. Additionally, numerous SIS/PIB-based HCDs were prepared with six hydrophilic polymers, and their wound dressing properties were assessed. Finally, the wound healing efficacy of the selected formulations was compared to a commercial wound dressing. The swelling ratio, bioadhesive force and mechanical strengths of HCDs were increased in the order of sodium alginate > sodium CMC = poloxamer = HPMC > PVA = PVP, sodium alginate > sodium CMC = poloxamer > PVA> HPMC = PVP and sodium alginate ≥ PVA >PVP = HPMC = sodium CMC > poloxamer, respectively. Among the hydrophilic polymers tested, sodium alginate most enhanced the swelling capacity, bioadhesive force and mechanical strengths. Thus, the hydrophilic polymers played great role in the swelling, bioadhesion and mechanical strength of SIS/PIB-based HCDs. The HCD formulation composed of PIB, SIS, liquid paraffin and sodium alginate at the weight ratio of 20/25/12/43 gave better wound dressing properties and more excellent wound healing efficacy than the commercial wound dressing. Therefore, the novel HCD formulation could be a promising hydrocolloid system for wound dressings.

1. Introduction

A wound means a disruption or injury of skin structure and function, and gives the damage of intrinsic skin barriers (Boateng et al., 2015; Boateng and Catanzano, 2015). Wound healing is the gradual refurbishment of bruised tissues (Boateng et al., 2008). Moist wounds are less susceptible to infection than dry ones, because moisture around the wound accelerates tissue restoration and cosmesis, alleviates pain and resists microbial attack (Archana et al., 2013; Boateng et al., 2015; Kim et al., 2015). An ideal wound dressing is capable of: (a) providing an adequately prolonged close contact between dressing and skin area around the wound, (b) absorbing extra secretions exuded from the wound, (c) maintaining moist milieu around the wound, (d) letting the air go across, (e) ensuring protection from heat, and (f) detaching slickly without causing distress to the wound (Jayakumar et al., 2011). Common wound dressings, such as cotton wool, bandages or gauzes, do not provide these qualities sufficiently (Boateng et al., 2008). Conversely, a number of modern wound dressings, based on collagen, alginates, polyurethane, silicone, polyacrylates, chitosan or/and gelatin heal the wound quickly and without pain by maintaining adequate dampness and a shield around the wound (Archana et al., 2013; Boateng et al., 2015; Mohamad et al., 2014; Pawar et al., 2014). However, many of these modern wound dressings possess some disadvantages, such as inadequate swellability to absorb excess wound exudations, insufficient

* Corresponding author. Fax: +82 31 400 5958.
** Corresponding author. Fax: +82 53 810 4654.
E-mail addresses: jongohkim@yu.ac.kr (J.O. Kim), hangon@hanyang.ac.kr (H.-G. Choi).
[1] Both authors contributed equally to this work.

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strength to overcome stress caused by skin movement and deficient flexibility; therefore, the exploration of an ideal wound dressing is still ongoing. In addition, until now, most previous studies have been focused on developing a wound dressing system using a number of polymers. However, there has been lack of knowledge on the comparative effect of polymers on the wound dressing properties, even though the polymeric constituents play an important role in wound dressing properties.

The goal of the current study was to investigate the influence of different hydrophilic polymers on the swelling, bioadhesion and mechanical strength of hydrocolloid wound dressings in order to provide an appropriate composition of the hydrocolloid wound dressing system. In this study, the hydrocolloid wound dressings (HCDs) were prepared with styrene-isoprene-styrene copolymer (SIS) and polyisobutylene (PIB) as the base using a hot melting method. The hot melting method is a well-known way of fabricating transdermal adhesive drug delivery systems (Kim et al., 2015; Webster, 1997). SIS and PIB are hydrophobic polymeric entities which are perfect to be used as hot melt pressure-sensitive adhesives and elastomers owing to their stability at high temperatures and pressures, inertness to various drugs and inexpensiveness (Hughes and Looney, 1987; Jones et al., 2006). PIB contains a hydrocarbon structure which makes them chemically inert and resistant to weathering, higher temperatures and chemicals; accordingly, they are popular in the formulation of transdermal drug delivery systems (Jin et al., 2015a). Moreover, numerous HCDs were prepared with various hydrophilic polymers, and their swelling ratio, bioadhesive force and mechanical strength were assessed. In this comparative study, sodium alginate (Choi and Kim, 2000; Kim et al., 2008a,b), sodium carboxymethyl cellulose (Lim et al., 2010), hydroxypropyl methylcellulose (Yousaf et al., 2015), polyvinyl alcohol (Choi et al., 2014; Lim et al., 2010), polyvinylpyrrolidone (Yousaf et al., 2015) and poloxamer (Din et al., 2015) were used as the hydrophilic polymers with different nature and charges (Choi et al., 2014; Kim et al., 2008a, b). Finally, the wound dressing properties and wound healing efficacy of the selected formulations were compared to a commercial wound dressing (Jin et al., 2015a,b). Recently, chronic wounds are the primary challenges in the development of wound healing products, because these wounds contains the diabetic and leg ulcers, amputations, and traumatic and surgical wounds in which the infection and complications risks are very high (Boateng et al., 2015; Boateng and Catanzano, 2015). Thus, in this study, the diabetic induced rats were used as the animal model for evaluation of wound healing.

2. Materials and methods

2.1. Materials

Styrene-isoprene-styrene copolymer (SIS, Quintac®) was purchased from Zeon Co. (Tokyo, Japan). Polyisobutylene (PIB, Oppanol® B 15 SFN), polyvinylpyrrolidone (PVP) and poloxamer (P 407) were provided by BASF (Ludwigshafen, Germany). Liquid Paraffin was bought from Kukdong Oil & Chemical Co. (Yangsan, Korea). Sodium carboxymethyl cellulose (sodium CMC) was supplied from Akzo Nobel Functional Chem., Co. (Herkenbosch, Netherlands). Sodium alginate was purchased from Aldrich Co. (Milwaukee, WI, USA). Hydroxypropyl methylcellulose (HPMC) and polyvinyl alcohol (PVA) were procured from Shin-Etsu Co. (Tokyo, Japan). The backing layer and release liner were kindly supplied by Young chemical Co. (Yangsan, Korea). Duoderm™ (a commercial wound dressing) was purchased from Convatec Co. (Greensboro, NC, USA). All other chemicals were used without any further purification.

2.2. Animals

Male CrlOri:SKH1-hr strain hairless mice weighing 25–30 g and male SD rats weighing 250–280 g were used for the evaluation of bioadhesive force and *in vivo* wound healing effect, respectively. All animal care and procedures were implemented consistent with the NIH Policy and Animal Welfare Act under approval by the Institutional Animal Care and Use Committee (IACUC) at Hanyang University.

2.3. Preparation of hydrocolloid wound dressings (HCDs)

The HCDs were prepared by the hot melting method. The SIS was liquefied at 170 °C. The PIB was added to it when the melt cooled to 120 °C. Then, both the components were thoroughly mixed by mechanical stirring at 300 rpm for 30 min. The resultant transparent mixture was further cooled to 100 °C. Subsequently, liquid paraffin and hydrophilic polymer were added to it and stirred at 300 rpm for 20 min. The resultant hydrocolloid mixture was degassed and put onto a backing layer employing a hot melt coater (HLC-101, ChemInstruments; Mentor, OH, USA). The instrument was adjusted at a temperature of 100 °C and HCD thickness of 0.5 mm. Then, the release liner was added with a Benchtop Laboratory Laminator (LL-100, ChemInstruments; Mentor, OH, USA) in an air pressure of 20 psi. The detailed compositions of HCDs are given in Table 1.

2.4. Determination of swelling ratio

The square-shaped hydrocolloid samples (2cm × 2 cm) were dried at 60 °C for 12 h under vacuum, and the weight of each dry sample (W_{dry}) was determined. Subsequently, each dry sample was soaked in phosphate buffer (pH 7.4) at 37 °C for 24 h, and the weight of swollen sample ($W_{swollen}$) was determined. The swelling ratio (SR) was calculated using the following formula: $SR\ \% = (W_{swollen}/W_{dry}) \times 100$ (Kim et al., 2008a,b).

2.5. Determination of tensile strength and elongation at break

The tensile strength and elongation at break of the hydrocolloid samples (square-shape; 2cm × 2 cm) were assessed using a texture analyser (TA.XT2, Haslemere; Surrey, UK). The mechanical strength was evaluated by progressively cumulating the weight load until the hydrocolloid film ruptured. The lowest weight load which resulted in hydrocolloid film breakage was recorded. Furthermore, elongation at break (%) was determined by comparing the initial length (before stretch by the instrument) of hydrocolloid film and

Table 1
Compositions of hydrocolloid wound dressings.

Ingredient (weight, %)	I	II	III	IV	V	VI	VII
PIB	20	15	10	20	20	20	20
SIS	25	30	35	25	25	25	25
Sodium CMC	55	55	55	51	47	43	39
Liquid paraffin	–	–	–	4	8	12	16