MECHANICAL PROPERTIES AND WATER VAPOUR PERMEABILITY OF FILM FROM HARUAN *(Channa striatus)* AND FUSIDIC ACID SPRAY FOR WOUND DRESSING AND WOUND HEALING

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ABSTRACT

Aerosol is a new dosage form for wound dressing and wound healing. Concentrate of aerosols which were prepared for wound dressing and wound healing will produced films after sprayed onto the surface of wounds. The aim of this study is to evaluate the mechanical and water vapour permeability properties of the films from the aerosol concentrates. Film forming dispersions contained Haruan extract and Fusidic acid as the active ingredients, hydroxypropyl methylcellulose (HPMC) as polymer and polyethylene glycol (PEG) 400, glycerin and propylene glycol as plasticizers. Haruan extract is used to promote healing and Fusidic acid is added in formula as antibiotic to prevent the infections. The films were prepared by using casting technique. Based on the results, it is concluded that films produced from Formula E1, E2 and F4 possessed good elongation at break but low tensile strength. All Formula E, Formula F4 and F5 were permeable but Formula F5 was brittle and would peel off by themselves from the Petri dish.

Keywords: Haruan; *Channa striatus;* aerosol; film; mechanical properties; water vapour permeability.

INTRODUCTION

Aerosol (spray) as a drug delivery system has several benefits when compared with other delivery systems such as plasters and bandages for wound dressing and cream or gel for wound treatment. The benefits and the innovativeness of the aerosol compared to the technology currently available are: (a) the aerosol is easy to apply medical product onto any size of wound area without touching the wound physically compared to the currently available cream or gel, (b) the plasters have limited size, singly packaged and cause sufferings and pains to the patient during the dressing and removal processes, (c) the plasters are easily contaminated when removed from the pack, (d) in the aerosol system, the product remain sterile because no foreign material can go into the container (Sciarra, 1976; Sciarra & Cutie, 1990).

In this study, aerosol was formulated with Haruan extract which will be used as promote healing process and Fusidic acid as antibiotic to prevent the infection of wound. Aerosol with Haruan extract will be sprayed to the wound part of body, than it produces a thin films which will cover the wound. The dosage of active ingredient is delivered to the wound over time from the moist formulation and then from the dry film. The films were composed by polymer which was contained in concentrates of aerosol. This paper explains about mechanical and water vapour permeability properties of films from the aerosol concentrates.

MATERIALS AND METHODS

Materials

Haruan extract was acquired from Major Interest Sdn. Bhd. (Malaysia), Hydroxypropyl methylcellulose (HPMC H9262 manufactured by Sigma-Aldrich, Inc., St. Louis, USA) and α-tocopherol (Vitamin E) were supplied from Sigma-Aldrich Sdn. Bhd. (Malaysia). Fusidic acid was supplied by CM Meditech, Sdn. Bhd. (Malaysia). Polyethylene glycol (PEG) 400 was purchased from Merck-Schuchardt. Propylene glycol, glycerin, methyl paraben, and propyl paraben were acquired from R&M Chemicals, Essex (U.K.). Ethanol was bought from Systerm AR. All chemicals were used without further purification.

Methods

Preparation of films from the aerosol concentrates

Casting techniques were used for films preparation (Pongjanyakul & Puttipipatkhachorn, 2008). Specified quantities of methyl paraben (0.1%), propyl paraben (0.02%), and α-tocopherol (0.01%) were dissolved in 20% ethanol. HPMC (2%), plasticizer (E1 = PEG 400, E2 = glycerin and E3 = propylene glycol) (1%) and Haruan extract (20%) were added and dispersed into the solution and mixed. The weights of the dispersions were made up to 100 % by the addition of ethanol. For formula F, Fusidic acid (2%) was added into dispersion after Haruan extract. F1, F2, F3, F4, F5 and F6 formulas used PEG 400 (1%), glycerin (1%), propylene glycol (1%), PEG 400 (2%), glycerin (2%) and propylene glycol (2%)

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respectively as plasticizer. The dispersions were homogenized by using ultra turrax (IKA T18 Basic) at 10,000 rpm for 15 minutes. Ten grams of homogenised dispersions or concentrates were spread into 9.5 cm diameter Petri dishes and dried at room temperature for 24 hours. The films were evaluated based on its ease of formulation and physical appearance.

Film thickness

The film thicknesses were measured using a micrometer (Digimatic micrometer, Mitutoyo, Tokyo, Japan) by the method of Yoo *et al.* (2006). Sample with air bubbles, nicks or tears and having mean thickness variations of greater than 10% were excluded from analysis (Macleod *et al*., 1997).

Mechanical properties measurements

The mechanical properties of aerosol concentrate films were evaluated using a texture analyzer (TA.XT2, Stable Micro System, Haslemere, Surrey, UK) by the method of Khan *et al.* (2000). The tensile strength and elongation at break were calculated as below:

$$\text{Tensile strength (N/mm}^2) = \frac{\text{Breaking Force (F)}}{\text{Cross sectional area of sample (A)}}$$

$$\text{Elongation at break (\%)} = \frac{\text{Increase in length at breaking point (L - Lo)}}{\text{Original length (Lo)}} \times 100\%$$

Cross section area of sample (mm^2) = [width of the test film (mm)] x [thickness of the test film (mm)]. Lo = original length (mm), L = length at breaking point (mm)

Young's modulus (E), a measure of intrinsic film stiffness (Garcia *et al*., 2009), can be calculated by using the following equation (Martin *et al*., 2001):

$$\frac{F}{A} = E \frac{(L - Lo)}{Lo}$$

$$\text{Young's modulus (N/mm}^2) = \frac{\text{Tensile Strength (N/mm}^2)}{\text{Elongation at break}}$$

Water vapour permeability of films

The rates of water vapour permeability of films were determined using the method described in USP XXIV (2000) for the evaluation of moisture permeability of containers and packaging materials. Films were tied onto the mouth of small glass bottles of the same size and type (diameter = 1.6 cm) with an average volume of 25 ml ± 0.5 ml. The average area available for vapour permeation was 2.0096 cm^2. The rate of moisture permeability was calculated by using the equation:

$$\text{Rate of moisture Permeability (mg/day/litre)} = \frac{1000}{14\,V} \times [(Tf - Ti) - (Cf - Ci)]$$

Which V is volume (ml) of the container, (Tf – Ti) is the difference (mg) between the final and initial weights of each test container, (Cf – Ci) is the average of the difference (mg) between final and initial weights of two containers (control).

STATISTICAL ANALYSIS

The results were represented as mean ± SD, treated statistically by using SPSS software (version 15, USA).

Table 1: The visual evaluation of the films formula E and formula F

Formula	Physical properties of film formed	Appearance of the film formed
E1	Could be peeled off easily from the plate	Transparent, soft and tough, flexible and pliable film with smooth surface and free from any precipitation or air pockets
E2	Could be peeled off easily from the plate	Transparent, soft and tough, flexible and pliable film with smooth surface and free from any precipitation or air pockets
E3	Could be peeled off easily from the plate	Transparent, soft and tough, flexible and pliable film with smooth surface and free from any precipitation or air pockets
F1	Could be peeled off easily from the plate	Opaque film, slightly brittle and free from any precipitation or air pockets
F2	Peel themselves from the Petri dish	Opaque film, slightly brittle and free from any precipitation or air pockets
F3	Could be peeled off easily from the plate	Opaque film, slightly brittle and free from any precipitation or air pockets
F4	Could be peeled off easily from the plate	Opaque, soft and tough, flexible and pliable film and free from any precipitation or air pockets
F5	Peel themselves from the Petri dish	Opaque film, slightly brittle and free from any precipitation or air pockets
F6	Could be peeled off easily from the plate	Opaque film and free from any precipitation or air pockets

One-way analysis of variance was used to compare the results. Post-hoc Tukey Honestly Significant Difference (Tukey-HSD) test was applied when there was a statistically significant difference ($P<0.05$) (Khan *et al*., 2000; Petersen, 1985).

RESULTS AND DISCUSSION

Appearance of the films

The results of visual evaluation of the films prepared with the inclusion of Haruan extract (formula E), Haruan extract and Fusidic acid (formula F), and the selected plasticizer (1 and 4 = PEG 400, 2 and 5 = glycerin, or 3 and 6 = propylene glycol) were tabulated and presented as in table 1.

From table 1, it can be inferred that formula E produced transparent film, flexible and pliable, whereas incorporating Fusidic acid (formula F) gave opaque film and slightly brittle (formula F1, F2, F3 and F5). Films from formula F1, F3, F4 and F6 could be peeled off easily from the plate while films from formula F2 and F5 peeled off by themselves from the Petri dish. Formula E used plasticizer 1% whereas for formula F it is not enough. Films produced from the formula F with 1% plasticizer were smooth but slightly brittle. Therefore, concentration of plasticizer was improved to 2%.

Films thickness

The thickness of films from formula E and formula F is shown in Table 2. There were no significant different in films thickness of formula E ($P>0.005$), whereas incorporating Fusidic acid increased the films thickness.

Table 2: Films Thickness, Mean ± SD, N = 5

Formula	Films Thickness (mm)
E1	0.048^{a} ± 0.003
E2	0.048^{a} ± 0.003
E3	0.046^{a} ± 0.004
F1	$0.084^{b,c}$ ± 0.004
F2	$0.087^{b,c}$ ± 0.004
F3	0.080^{b} ± 0.007
F4	$0.086^{b,c}$ ± 0.005
F5	0.089^{c} ± 0.002
F6	$0.082^{b,c}$ ± 0.003

Means within a column with a different letter are significantly different ($P<0.05$)

Mechanical Properties Measurements

Humidity has significant effects on mechanical properties of films. HPMC films stored at 10% relative humidity had higher tensile strength than films stored at 80% relative humidity, but lower elongation at break (Radebaugh, 1992). From mechanical properties measurements, it is obtained tensile strength, elongation at break of film and Young's modulus. The mechanical properties of formula E1, E2, and E3 films are given in table 3 and formula F1, F2, F3, F4, F5 and F6 films are given in table 4.

The results in table 3 showed that tensile strength, elongation and Young's modulus of formula E1 and E2 were not significantly different ($p>0.05$), whereas formula E3 was significantly different with the other two formulas. Formula E3 has the highest tensile strength and Young's modulus; and the lowest elongation at break. It is mean that propylene glycol could not increase the elasticity of films while films produced were strong. Tensile strength showed a similar trend than Young's modulus results. On the other hand, Young's modulus showed an opposite behaviour to elongation at break.

It is supposed that the wound dressing film is preferable to be sturdy but pliable (Khan *et al*., 2000; Macleod *et al.,* 1997, Nagarsenker & Hegde, 1999) and the ideal dressing film should be elastic (Sezer *et al.,* 2007) .

Table 3: Mechanical properties of aerosol concentrate films from formula E at RH 50%, Mean ± SD, N = 6

Formula	Tensile Strength (N/mm^2)	Elongation at Break (%)	Young's Modulus (N/mm^2)
E1	15.68^{a} ± 0.50	36.93^{b} ± 4.56	43.01^{a} ± 5.70
E2	15.09^{a} ± 1.43	39.70^{b} ± 7.82	39.15^{a} ± 8.00
E3	28.17^{b} ± 1.55	7.61^{a} ± 1.30	381.99^{b} ± 83.70

Means within a column with different letter are significantly different ($P<0.05$)

Table 4: Mechanical properties of aerosol concentrate film from formula F at RH 50%, Mean ± SD, N = 6

Formula	Tensile Strength (N/mm^2)	Elongation at Break (%)	Young's Modulus (N/mm^2)
F1	21.59^{c} ± 0.94	$5.66^{a,b}$ ± 0.74	386.18^{b} ± 48.18
F2	27.29^{d} ± 0.80	3.76^{a} ± 0.39	731.83^{c} ± 69.38
F3	22.00^{c} ± 3.39	2.36^{a} ± 0.14	931.59^{d} ± 122.94
F4	9.15^{a} ± 0.88	38.31^{d} ± 3.16	23.90^{a} ± 1.26
F5	10.12^{a} ± 0.32	9.16^{b} ± 1.46	112.64^{a} ± 15.95
F6	13.44^{b} ± 1.15	25.70^{c} ± 3.78	62.78^{a} ± 10.71

Means within a column with different letter are significantly different ($P<0.05$).

The percentage of elongation decreased with added the Fusidic acid to the formula with the same percentage and plasticizer, indicating that the HPMC cast film becomes brittle due to the added Fusidic acid (Nakano & Yuasa, 2001). The percentage of elongation will increase if percentage of plasticize increases (table 4). The brittleness of the film was indicated by low values for elongation at break (Macleod *et al.,* 1997). Percentage plasticizer also affected tensile strength. The tensile strength decreased when the percentage of plasticizer increased (Yoo *et al*., 2006).

Water Vapour Permeability

The ideal wound dressing should has several characters, such as ability to control gases diffusion, maintains a moist environment around the wound, prevent further inflammation, simple and easy to use with little or no pain from the wound, cosmetically acceptable and cost effective (Balakrishnan *et al*., 2005; Cockbill, 2007; Watson & Hodgkin, 2005; Weiss *et al*., 1993). The wound dressing films have to be permeable to control the moisture and gases in order to help in the wound healing process (Santos *et al*., 2006; Turner, 1991). Table 5 and 6 show the water vapour permeability of films from formula E and F. Water vapour permeability of films was significantly decreased with added Fusidic acid into formula. Thickness and water vapour permeability of films vary in inverse proportion.

Table 5: Water Vapour Permeability of films from formula E, Mean ± SD, N = 10

Formula	Water vapour permeability (mg/day/litre)
E1	$3468.49^{b} \pm 227.99$
E2	$3457.89^{b} \pm 171.92$
E3	$2254.18^{a} \pm 249.02$

Means within a column with a different letter are significantly different (P<0.05)

Table 6: Water Vapour Permeability of films from formula F, Mean ± SD, N = 10

Formula	Water vapour permeability (mg/day/litre)
F1	$774.46^{c} \pm 77.31$
F2	$705.66^{c} \pm 12.20$
F3	$579.03^{b} \pm 155.67$
F4	$2524.18^{d} \pm 50.09$
F5	$2438.52^{d} \pm 103.84$
F6	$426.38^{a} \pm 43.75$

Means within a column with a different letter are significantly different (P<0.05)

According to USP XXIV (2000), the containers were categorized as tight containers if results showed that no more than one of the 10 test containers exceeded 100 mg/day/litre in moisture permeability, and categorized as well-closed containers if not more than one of the 10 test containers exceeded 2000 mg/day/litre. As such, the results obtained suggested that all film from Formula E and Formula F4 and F5 were permeable and other formula F were well-close or not permeable to moisture.

CONCLUSION

From this study, it is concluded that films produced from Formula E1, E2 and F4 possessed good elongation at break but low tensile strength. All Formula E, Formula F4 and F5 were permeable but Formula F5 would peel by themselves from the Petri dish and brittle.

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