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Characterization of Natural Rubber Latex Film Containing Various Enhancers

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Abstract

Natural rubber latex (NRL) is often used to prepare the blended films by solution-casting technique. Its film presents interesting physical properties in elasticity and adhesiveness. From the good physical properties of NRL, it can be used to prepare transdermal patches which gain popularity due to several advantages such as convenient application, avoid first-pass metabolism, possibly to attain sustained and constant drug levels. However, the skin serves an excellent barrier against drug permeation due to the rigid lamellar structure of the stratum corneum lipids. Enhancers can improve the partition of drug into the stratum corneum by increasing the thermodynamic activity of the drug in transdermal formulations. The aims of this study were (i) to prepare the blended films from deproteinized NRL (DNRL), hydroxypropylmethyl cellulose (HPMC), dibutyl phthalate (DBP), various enhancers, i.e., fatty acid (oleic acid), ester of fatty acid (isopropyl palmitate; IPP), fatty alcohol (propylene glycol; PG), hydrocarbon (olive oil), and terpene (menthol), and (ii) to study the physical and mechanical properties of the obtained films. The results showed that DNRL could be compatible with all enhancers. Hence, the blended films were characterized for strength (ultimate tensile strength; UTS), elasticity (elongation at break), and adhesiveness (peel strength and tack adhesive). It was found that these characteristics depended on type and concentration of incorporated enhancers.

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Keywords: Natural rubber latex; film; enhancer; transdermal; mechanical properties.

1. Introduction

The latex from *Hevea brasiliensis*, the commercial source of natural rubber, is composed of about 30% rubber fraction, 5% non-rubber, and water. Natural rubber latex (NRL), consists mainly *cis*-1,4

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polyisoprene, has been widely used as film formulations in many applications such as tubing, balloon, and glove. By reason of its excellent elasticity, flexibility, tack, and high surface friction [1,2], it can be used to develop for transdermal patch preparations in pharmaceutical applications. Deproteinized NRL (DNRL) was prepared by enzymatic deproteinization to remove the protein from fresh NRL resulting in the reduction of latex allergy problems [3,4]. In our previous report, the mixed ingredients of DNRL and hydroxypropylmethyl cellulose (HPMC) as blended polymers, and dibutyl phthalate (DBP) as plasticizer, provided the suitable matrix transdermal patches [5]. However, the skin serves an excellent barrier against drug permeation due to the rigid lamellar structure of the stratum corneum lipids. Enhancers can improve the partition of drug into the stratum corneum by increasing the thermodynamic activity of the drug in the transdermal formulations [6]. Therefore, the aims of this study were (i) to prepare the blended films from DNRL, HPMC, DBP, various enhancers, i.e., fatty acid (oleic acid), ester of fatty acid (isopropyl palmitate; IPP), fatty alcohol (propylene glycol; PG), hydrocarbon (olive oil), and terpene (menthol), and (ii) to study the physical and mechanical properties of the obtained films.

2. Experiment

2.1. Materials

DNRL was prepared from the fresh NRL that collected from *Hevea brasiliensis* (RRIM 600 clone) via the technique developed by our group [5]. HPMC was obtained from Onimax (China). DBP was obtained from Sigma-Aldrich (USA.). Oleic acid, IPP, PG, olive oil and menthol were purchased from P.C. Drug Center (Thailand). All chemicals were pharmaceutical grade and used as received.

2.2. Preparation of film formulations

The 10%w/v HPMC was prepared by dissolving HPMC in distilled water. Various concentrations (5, 10, 15 and 20 phr) of each enhancer (oleic acid, IPP, PG, olive oil, or menthol) were mixed with DBP. All components were then homogeneously mixed (Table 1). Then, the formulations were kept in an ultrasonic bath for 30 minutes (Crest CP 1100, USA) to eliminate air bubbles. The films could be prepared by pouring the formulations into a Petri-dish and dried by hot air oven (Mammert 100-800, Germany) at 45 ± 2 °C for overnight. Each film was laid on wax paper separately, and stored in desiccators.

2.3. Film characterizations

Thickness. The thickness of films was measured at five different areas using a micrometer (Teclock corporation, Japan), and the mean as well as standard deviation values were calculated.

Tensile strength. Tensile strength was determined in term of Young's modulus, ultimate tensile strength (UTS), and elongation at break using an Instron testing machine (model 5569, Instron Corporation, USA.) with a 500N loaded cell following the method modified from the ASTM D412 [7]. Films were cut into the rectangular specimens of 10×30 mm². The gauge length was set at 10 mm and the cross-head speed was controlled at 10 mm/min. The Young's modulus, which is the manifestation of stiffness of a material, was calculated from the initial slope of the stress-strain plot within the range of elastic limit of stretching. The UTS was expressed as the maximum force at break divided by the initial cross-sectional area of the film strip, and the elongation at break as a percentage of the original length. These tensile values were calculated by equation 1-3, respectively.

$$\text{Young's modulus} = \frac{\text{Stress}}{\text{Strain}} \quad (1)$$

$$UTS = \frac{F}{A} \quad (2)$$

$$\% \text{Elongation at break} = \frac{(L_s - L_0)}{L_0} \times 100 \quad (3)$$

where; F is breaking load (N)

A is cross section area of the specimen (width \times thickness, mm^2)

L_0 is original length of the specimen (mm)

L_s is length at breaking point of the specimen (mm)

Peel strength. Peel strength was determined by means of a T-peel method modified from the ASTM D1876 [8] using transparent polyvinyl chloride sheet as substrate. Measurement of the force required to peel specimen away from transparent sheet was performed by using an Instron testing machine with a 500N loaded cell which the size of film specimens was $10 \times 60 \text{ mm}^2$. The cross-head speed was controlled at 300 mm/min dwell time.

Table 1. Composition of the Formulations

Code	DNRL (phr)	HPMC (phr)	DBP (phr)	Oleic acid (phr)	IPP (phr)	PG (phr)	Olive oil (phr)	Menthol (phr)
F0 (Control)	100	10	5	-	-	-	-	-
F1	100	10	5	5	-	-	-	-
F2	100	10	5	-	5	-	-	-
F3	100	10	5	-	-	5	-	-
F4	100	10	5	-	-	-	5	-
F5	100	10	5	-	-	-	-	5
F6	100	10	5	10	-	-	-	-
F7	100	10	5	-	10	-	-	-
F8	100	10	5	-	-	10	-	-
F9	100	10	5	-	-	-	10	-
F10	100	10	5	-	-	-	-	10
F11	100	10	5	15	-	-	-	-
F12	100	10	5	-	15	-	-	-
F13	100	10	5	-	-	15	-	-
F14	100	10	5	-	-	-	15	-
F15	100	10	5	-	-	-	-	15
F16	100	10	5	20	-	-	-	-
F17	100	10	5	-	20	-	-	-
F18	100	10	5	-	-	20	-	-
F19	100	10	5	-	-	-	20	-
F20	100	10	5	-	-	-	-	20

Tack adhesion. Tack adhesion measurement as loop tack method was modified from the ASTM D6195 [9] and evaluated by using an Instron testing machine with a 500N loaded cell. The loop tack of the

adhesive was contacted with stainless steel surface as substrate and separated on vertical jaw of rate 300 mm/min dwell time. The size of film specimens was $25 \times 60 \text{ mm}^2$.

3. Results and Discussion

From the deproteinization process, the total protein content in DNRL, determined by Kjeldahl methods as described in ASTM D3533 [10], was reduced for more than 89.22% comparing with that in the fresh NRL [5]. DNRL blended with HPMC, DBP, and various enhancers could form the yellowish transparent films. The physical and mechanical properties of the DNRL blended films are shown in Table 2. The thickness ranged between 0.27-0.43 mm. Their low standard deviation values indicated that the films were uniform in thickness.

Table 2. Physical and mechanical properties

Code	Thickness (mm)	Modulus (MPa)	UTS (MPa)	Elongation at break (%)	Peel strength (N/cm)	Tack adhesion (N/cm)
F0 (Control)	0.37±0.01	1.51±0.08	0.34±0.06	1452.39±119.27	0.34±0.02	0.16±0.01
F1	0.40±0.02	1.08±0.11	0.19±0.02	1394.44±114.47	0.42±0.02	0.12±0.01
F2	0.32±0.02	0.75±0.10	0.08±0.01	1261.1108±206.49	0.32±0.04	0.10±0.01
F3	0.34±0.03	1.01±0.16	0.05±0.01	613.89±121.30	0.36±0.03	0.10±0.01
F4	0.37±0.02	0.83±0.11	0.04±0.01	789.17±122.22	0.46±0.04	0.08±0.01
F5	0.27±0.01	1.29±0.16	0.32±0.04	1122.50±142.26	0.37±0.02	0.08±0.01
F6	0.29±0.02	1.28±0.21	0.27±0.01	1046.67±81.90	0.39±0.04	0.06±0.01
F7	0.42±0.01	1.17±0.13	0.28±0.03	1494.17±122.91	0.48±0.05	0.11±0.01
F8	0.38±0.01	1.46±0.10	0.33±0.03	1349.86±120.25	0.37±0.03	0.08±0.01
F9	0.41±0.02	1.76±0.15	0.36±0.03	1108.60±170.43	0.25±0.03	0.11±0.01
F10	0.32±0.02	1.11±0.21	0.17±0.03	1069.17±231.23	0.34±0.03	0.14±0.01
F11	0.43±0.01	1.13±0.17	0.28±0.04	1114.27±188.24	0.41±0.04	0.13±0.01
F12	0.32±0.01	0.96±0.12	0.26±0.03	1553.06±194.06	0.32±0.03	0.06±0.01
F13	0.33±0.02	0.95±0.08	0.18±0.02	1186.94±133.39	0.25±0.01	0.06±0.01
F14	0.37±0.02	0.95±0.05	0.22±0.03	1310.00±190.75	0.19±0.03	0.07±0.01
F15	0.32±0.01	0.59±0.04	0.10±0.01	1307.77±124.77	0.19±0.02	0.05±0.01
F16	0.33±0.01	0.71±0.06	0.11±0.01	1049.44±10.73	0.16±0.02	0.06±0.01
F17	0.35±0.03	1.32±0.06	0.32±0.04	959.17±162.62	0.09±0.01	0.05±0.01
F18	0.34±0.02	1.50±0.21	0.42±0.03	931.36±131.67	0.09±0.01	0.06±0.01
F19	0.36±0.03	1.13±0.16	0.29±0.06	1447.78±133.54	0.08±0.01	0.09±0.01
F20	0.32±0.02	1.33±0.03	0.41±0.05	1010.56±164.08	0.16±0.02	0.07±0.01

The blended films containing various enhancers gave lower modulus values comparing with the control film (F0 as film without any enhancer). This result indicated that additive enhancers provided a softness films. The UTS of the blended films with various enhancers were lower than that of F0 film. UTS of F18 and F20 which contained 20 phr of PG and menthol, respectively, drastically increased which suggesting the immiscibility of the components. The elongation at break of most blended films, except F7 and F12 which contained 10 and 15 phr of IPP, respectively, decreased when comparing with the control film, indicating lower flexibility than control. The results suggested that IPP could improve the elasticity of blended films at appropriately concentrations, i.e., 10 and 15 phr. Adhesive properties (peel strength and tack adhesion) decreased in the blended films containing enhancers at high concentration as seen in

F16-F20. Therefore, DNRL blended films with very high concentration of enhancers were predicted that they were unsuitable for transdermal patches.

4. Conclusion

The blended films of DNRL, HPMC, DBP, and various enhancers could form appropriate films. The physical and mechanical properties of the blended films depended on type and concentration of enhancers. From the good elasticity of blended films, they could develop to apply as transdermal patches. In the future work, the properties of blended films should to be studied for the compatibility with Fourier transform infrared spectroscopy (FT-IR) and differential scanning calorimeter (DSC).

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References

- [1] Nakason C., Kaesaman A., Eardrod K., *Mater. Lett.* 2005; **59**: 4020-4025.
- [2] Rippel M.M., Lee L.T., Leite C.A.P., Galembeck F., *J. Colloid Interface Sci.* 2003; **268**: 330-340.
- [3] Kawahara S., Takano K., Isono Y., Yunyongwattanakorn J., Hikosaka M., Sakdapipanich J.T., Tanaka Y., *Polym. J.* 2004; **36**: 361-367.
- [4] Yeang H.Y., Arif S.A.M., Yusof F., Sunderasan F., *Methods* 2002; **27**: 32-45.
- [5] Suksaeree J., Boonme P., Taweepreda W., Ritthidej G.C., Pichayakorn W., *Chem. Eng. Res. Des.* 2011; doi: 10.1016/j.cherd.2011.11.002.
- [6] Singh A., Sharma P.K., Garg G., *Intl. J. Pharm.* 2010; **2**: 707-716.
- [7] ASTM International. Standard test methods for vulcanized rubber and thermoplastic elastomers-tension D412. ASTM International: West Conshohocken, Pennsylvania, United States. 2003; 9.
- [8] ASTM International. Standard test method for peel resistance of adhesives (T-peel test) D1876. ASTM International: West Conshohocken, Pennsylvania, United States. 2003; 15.
- [9] ASTM International. Standard test methods for loop tack D6195. ASTM International: West Conshohocken, Pennsylvania, United States. 2003; 15.
- [10] ASTM International. Standard test method for rubber-nitrogen content D3533. ASTM International: West Conshohocken, Pennsylvania, United States. 2003; 9.