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Formulations of Natural Rubber Latex as Film Former for Pharmaceutical Coating

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Abstract

Natural rubber latex (NRL) from *Hevea brasiliensis* consists of poly-*cis*-1,4-isoprene polymer displaying excellent physical properties such as high elasticity, high tensile strength, and ease of film-forming. However, the film casted from NRL is soft and sticky. The aim of this research was to apply the NRL as polymeric material for tablet coating. NRL, triethyl citrate (TEC) and titanium dioxide (TiO_2) were used as polymer, plasticizer and antiadherant, respectively. Mechanical properties of the casted films were characterized. It was found that TEC and TiO_2 affected the properties of the films. The results showed good compatibility which confirmed by Fourier transforms infrared (FTIR) spectroscopy. These results confirmed that NRL was possible to use as film former for pharmaceutical coating applications.

Keywords: Natural rubber latex; film former; pharmaceutical coating; mechanical property; compatibility.

1. Introduction

Natural rubber latex (NRL) obtained from *Hevea brasiliensis* is a colloidal system of poly-*cis*-1,4-isoprene particles dispersed in an aqueous serum. It presents interesting physical properties such as high elasticity, high tensile strength, and ease of film-forming. In freshly tapped latex, it contains about 30% rubber fraction which was concentrated by centrifugation to about 60% rubber content in commercial latex production and preserved with ammonia to against bacterial attack and to provide long-term stability through hydrolysis of phospholipids to fatty acid soaps [1-3].

Film coating technology has been widely used in pharmaceutical industries for many purposes such as preparation of film coated tablet, enteric coated tablets, controlled release tablet, etc. The objectives of

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film coating are to increase the stability of the drug, prevent the undesired taste of the drug, and control the drug release of pharmaceutical products as required for more effective treatment [4]. The key factor of production process is type of film forming agent [5,6]. In this study, NRL was applied as polymeric material for tablet coating by formulation with triethyl citrate (TEC) and titanium dioxide (TiO_2) as plasticizer and antiadherant, respectively. The feasibility of NRL for pharmaceutical coating application was evaluated.

2. Experiment

2.1. Materials

Commercial NRL concentrated or centrifuged latex (60% dry rubber content, DRC) with high ammonia was obtained from Chalong Latex Industry, Thailand. Triethyl citrate (TEC) was purchased from Aldrich, USA. Titanium dioxide (TiO_2) was purchased from Srichand United Dispensary, Thailand. The other chemicals were of analytical grade and used as received.

2.2. Preparation of NRL films

For studying effects of TEC, the film formulations were prepared by diluting the commercial NRL concentrated with distilled water to the final concentration of 10% DRC and mixing with 10, 15, or 20% TEC. For investigating effects of TiO_2, the film formulations were prepared by mixing commercial NRL concentrated with TiO_2 powder in the final concentration of 1, 2, or 5% based on DRC.

Each obtained mixture about 7-10 g was poured into a Petri-dish and transferred to hot air oven at 37 °C, 8 h for water evaporation. Subsequently, dry films were peeled off from Petri-dish and kept in desiccators until characterization for mechanical properties, i.e. Young's modulus, ultimate tensile strength (UTS), elongation at breaks, and tack adhesion and also for the compatibility of film compositions by Fourier transforms infrared (FTIR) spectroscopy.

2.3. Physicomechanical properties of NRL films

The methods used for evaluating mechanical properties were based on the guideline of the American Society for Testing Materials, ASTM. The film specimens were cut into rectangular shape and determined the mechanical properties using Instron testing machine (model 5569; Instron Corporation, USA) with a 500 N loaded cell. The mechanical studies of films were monitored by the tensile strength which modified from the ASTM D412 in terms of Young's modulus, UTS, elongation at break [7], and the adhesiveness in term of tack adhesion which modified from the ASTM D6195 [8].

Tensile strength was determined following the method which modified from the ASTM D412 [7]. The size of film specimens was 10×30 mm^2 which the gauge length of tested area was 10 mm. The cross-head speed was controlled at 10 mm/min. The Young's modulus, which is the manifestation of stiffness of a material, is calculated from the initial slope of the stress-strain plot within the range of elastic limit of stretching. The UTS is defined as either a distinct maximum or a region of strong curvature approaching zero-slope in the stress-strain curve. The elongation at break is determined by removing the fractured specimen from the grips, fitting the broken ends together and measuring the distance between gages makes. These mechanical properties were calculated by Equations 1-3.

$$\text{Young's modulus} = \frac{\text{Stress}}{\text{Strain}} \tag{1}$$

$$UTS = \frac{F}{A} \tag{2}$$

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

Where; F is breaking load (N)
A is cross section area of the specimen (width × thickness, mm^2)
L_0 is original length of the specimen (mm)
L_S is length at breaking point of the specimen (mm)

Tack adhesion is the force to separate the adhesive from the surface of another material at interface shortly after they have been brought into contact under a load equal only to the weight of the pressure-sensitive article on contact area by means of a loop tack method. In other words, it is a definition of the 'stickiness' of the adhesive. Too high tack adhesion may cause some problems in removing and refitting, while too low tack adhesion may lead to bond failure during application. Tack adhesion measurement was modified from the ASTM D6195 [8]. The loop tack of the adhesive was determined using stainless steel surface as substrate. The film specimen of 25 × 60 mm^2 was formed loop, clamped tape, pushed down on the substrate with specific force, and pulled off by a tensile tester and vertical jaw with separation rate of 300 mm/min dwell time.

2.4. Compatibility study of NRL films

The compatibility of film compositions was confirmed by FTIR spectroscopy. The prepared thin films were examined using Attenuated Total Reflection FTIR (ATR-FTIR) technique. They were scanned at a resolution of 4 cm^{-1} with 16 scans over wavenumber region peaks of IR transmission spectra of 400-4000 cm^{-1} using FTIR spectrophotometer (Perkin Elmer, USA). The characteristic peaks of IR transmission spectra were recorded.

2.5. Preliminary study for tablet coating

Film coating components were chosen from the formulation with optimized mechanical properties. Core tablets were prepared by wet granulation technique and weighed around 300 mg/tablet. A batch of 500 g core tablets was coated with the selected coating formulation using conventional coating pan-spray method in a standard coating pan coupled with an air-atomized spray nozzle.

3. Results and Discussion

3.1. Physicomechanical properties

The mechanical properties of each film formulation are shown in Figure 1. It was found that NRL films could form good elastic film (as high % elongation at break) with low adhesive property. Mixing NRL films with different amount of plasticizer and antiadherant formed satisfactory films with different mechanical properties. For NRL mixed with TEC films, the addition of TEC as plasticizer resulted in decreasing of the Young's modulus, tack adhesion but increasing UTS and elongation at break. For NRL mixed with TiO_2 films, the addition of TiO_2 as antiadherant resulted in increasing elongation at break. Mixed film with increasing amount of TiO_2 showed more brittle film but did not significantly affect to

Young's modulus from baseline. At 2% TiO_2 of NRL mixed film was the highest UTS and lowest tack adhesion.

From these results, NRL mixed with 20% TEC and 2% TiO_2 is the best film-coating solution for tablet coating in the preliminary study.

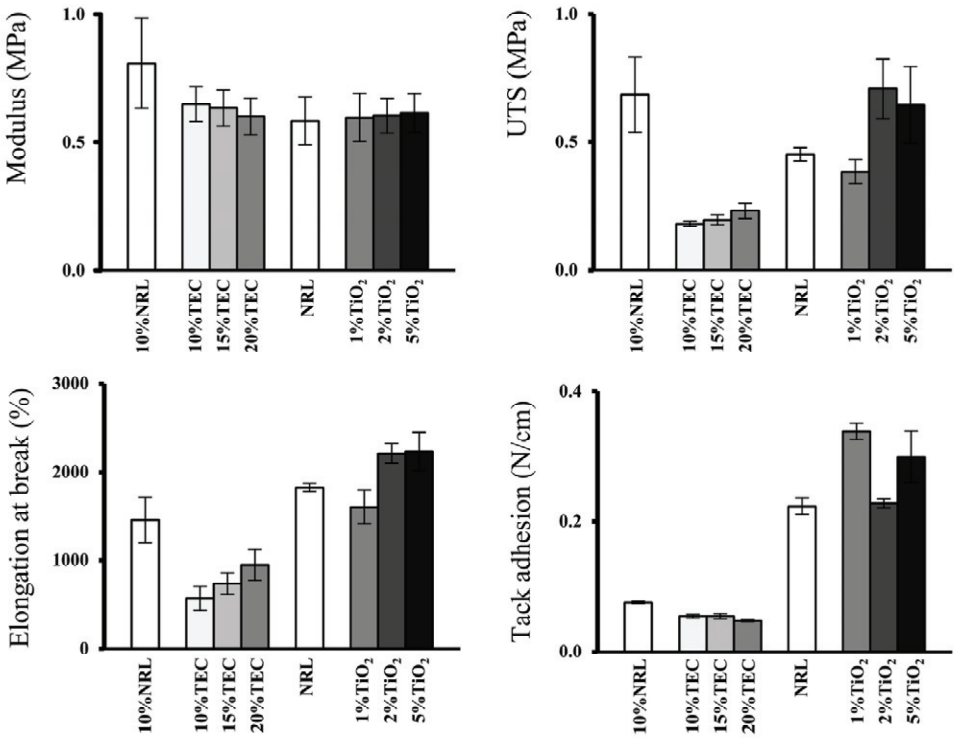

Fig. 1. Physicomechanical properties of NRL films mixed with TEC and TiO_2

3.2. Fourier transforms infrared spectroscopy study

The FTIR spectra of the NRL films and NRL films with additives are presented in Figure 2. The NRL spectrum was district the principal peak at 3036 cm^{-1} (=CH stretching), 2853-2961 cm^{-1} (C-H stretching), 1663 cm^{-1} (C=C stretching), 1376-1449 cm^{-1} (C-H bending) and 835 cm^{-1} (C=CH wagging) [1,9]. No markedly changeable spectrum was observed indicating no incompatibility of each ingredient in blended film.

3.3. Tablet coating

NRL film-coating solution was easy to be prepared and to spray through spray nozzle via the aqueous polymeric coating technique. NRL coated tablets were pale yellowish and glossy. The surface of the coated tablets exhibited smooth with uniform color.

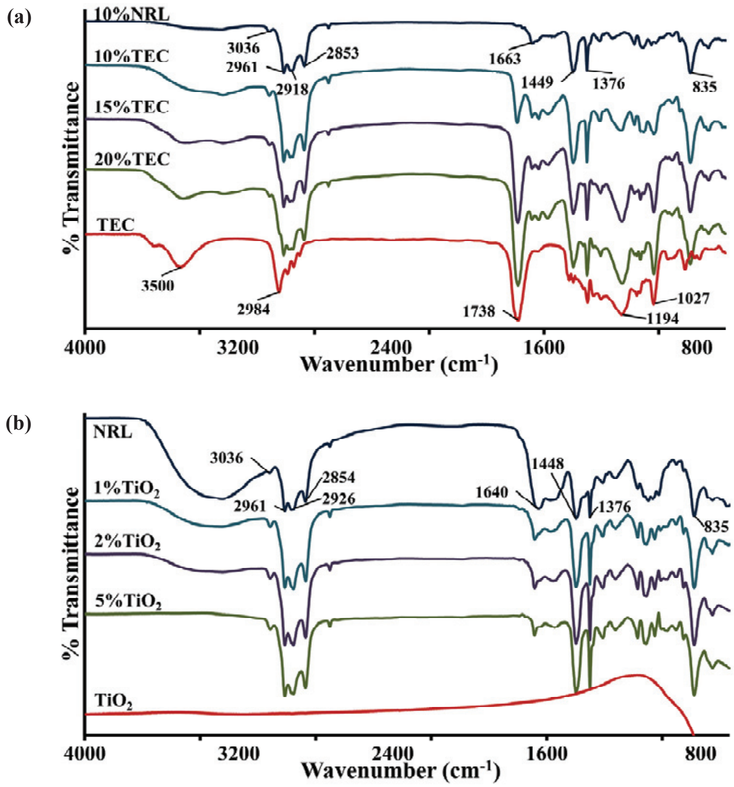

Fig. 2. Infrared spectra of NRL films mixed with (a) TEC and (b) TiO_2

4. Conclusion

Mechanical and adhesion properties of NRL films were depended on amount of TEC and TiO_2. Good compatibility among the components was confirmed by FTIR. NRL coating solution with optimized mechanical properties could be sprayed through spray nozzle while coating the core tablets. The results confirmed that NRL was possible to be used as film former for pharmaceutical coating applications. Future works will be focused to the investigation of the NRL coating performance and effects on release of a model drug.

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