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Development of *In Situ* Cooling Natural Rubber Film

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Abstract. Natural rubber latex (NRL) with the deproteinized process was interesting for cosmetic and transdermal drug delivery systems because of its notable characteristics. The purpose of this study was to develop *in situ* cooling films from deproteinized natural rubber latex (DNRL). Menthol, camphor, and volatile oils were added into DNRL emulsions for cooling effect and pain relief. The pH, rheological properties, particle size, and zeta potential of emulsions were examined. Then, the time of film-formation, morphology, and mechanical properties of the cooling NRL films were evaluated. The resultant emulsions revealed that their pH was about 5.7 - 6.3. The viscosity was in the range of 1000 – 3000 cps and indicated the pseudoplastic flow. The increasing amount of olive oil reduced the particle size and increased the negatively zeta potential of those emulsions. The film formation time of specimens was about 4.5 - 6.5 mins. The cooling films demonstrated smoothness and homogeneity. The presence of olive oil increased the softness of films. The increasing of oil volume increased the elasticity; however, it decreased the ductility of the films. This *in situ* cooling DNRL film was also effective forward for the development of a transdermal drug delivery system.

Introduction

Natural rubber latex (NRL) is a milky colloidal dispersion obtained from *Hevea brasiliensis*. NRL has many outstanding properties, including elasticity, toughness, abrasion resistance, adhesion, film-forming, hydrophobicity, etc. Therefore, NRL plays an essential role in engineering, medicine, and pharmaceuticals [1]. However, the NRL has reported latex allergies caused by 15 NRL proteins (Hev b1-15). The deproteinization process is used to remove those proteins from fresh NRL to decrease the risk of contact urticaria [2]. Deproteinized natural rubber latex (DNRL) is interesting to use in a few research as cosmetic and transdermal drug delivery systems [1,3].

Menthol is a selective activator of transient receptor potential melastatin-8 (TRPM8) channels and a vasoactive compound. In topical pharmaceutical formulation, menthol acts as a counter-irritant by imparting a cooling effect and initially stimulating nociceptors and desensitizing them. They may also activate central analgesic pathways [4]. The 30% menthol topical application has been reported to decrease cold pain thresholds and enhanced pain responses to suprathreshold noxious cold stimuli without affecting responses to other stimuli. The subject showed no sign of skin irritation or redness [5]. Camphor has been applied in the pharmaceutical field as an analgesic, antipruritic, antispasmodic, anti-inflammatory rubefacient, antiseptic, etc. It shows to activate heat-sensitive transient receptor potential (TRP) vanilloid subtypes 1 (TRPV1) and 3 (TRPV3). Camphor also activates the human cold-sensitive TRPM8 channel expressed in HEK293 cells. Hence, camphor induces both cold and warm sensations and improves blood circulation [6]. The topical of menthol and camphor is a combination medicine used to relieve minor muscle or joint pain.

This research aims to develop *in situ* cooling film from DNRL by adding menthol and camphor to relieve minor pain with the cooling effect and adding other volatile oils to pleasant to be used. Firstly, the emulsions were prepared. The pH, viscosity, rheology, particle size, and zeta potential of emulsions were evaluated. After that, the time of film-forming, morphology by scanning electron microscope (SEM), and mechanical properties by texture analysis of the cooling NRL films were determined.