Development of *Zingiber cassumunar* oil-Loaded Microneedle for Musculoskeletal Disorder

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Background: Musculoskeletal conditions are injuries or disorders of the muscles, nerves, tendons, joints, and cartilage. Globally, musculoskeletal disorders were found to be the most prevalent disease in 2019. Approximately 1.71 billion people with musculoskeletal disorders have been reported recently [1]. *Zingiber cassumunar* Roxb. (Plai) is a local medicinal herb in Asian countries. It has a strong benefit characteristic. For Thai traditional medicine, volatile oil from *Z. cassumunar* has been used to directly apply and penetrate the skin to remedy muscle stress and joint pain. In addition, this volatile oil has been used for a long time for the treatment of muscle inflammation according to its oil contains (*E*)-1-(3,4-dimethoxyphenyl) butadiene (DMPBD) as an active ingredient which proven to be an anti-inflammatory agent [2]. This volatile oil has been developed in various dosage forms such as cream or gel. However, these formulations require a long time for pain relief due to the slow penetration of drugs into the skin as a cause of the protective epithelial barrier. Therefore, a microneedle patch with micro-scale needles bypasses the stratum corneum to deliver molecules. Thus, providing painless skin insertion and effective muscle pain relief.

Methods: The essential oil of Z. *cassumunar* rhizomes is obtained by hydrodistillation using a Clevenger' s type apparatus with water at 130-150°C to obtain light yellowish oil. Dissolving microneedles (DMNs) were fabricated in a casting technique. The formulation consisted of volatile oil with poly (vinyl alcohol) (PVA) and poly (vinyl pyrrolidone) K32. DMNs were evaluated in terms of mechanical properties depending on the compression force test using a texture analyser. Further, insertion properties of DMNs were investigated using the parafilm M ® insertion test.

Results: All cone-shaped needles were formed entirely, sharp needles with a strong base plate and elegant appearance. A compression test was conducted to evaluate the mechanical strength that DMNs can withstand before they deform; after a 32-N compression, the average height reduction rates of the formulated displayed the height reduction with a value of 5.31 ± 0.32%. The force of 32-N was applied to assess the effects of insertion on needle height, using Parafilm M® as an artificial membrane to mimic the skin. It was found that volatile oil-loaded bilayer DMNs penetrated to the third layer of Parafilm M®. MN patches possessed the capability to be inserted into neonatal porcine skin, reaching insertion depths of approximately 250–300 μm. In the case of Parafilm M®, it was penetrated down to the third layer (approximately 370 μm. These results are very similar to previous insertion studies of polymeric MN into Parafilm M®.

Conclusions: The work presented here reports the successful formulation and mechanical characterization of dissolving microneedle arrays containing *Z. cassumunar* oil. Future work will focus on *in vitro* permeation of *Z. cassumunar* oil permeation using Franz cells.

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