Development of *Centella Asiatica* (Linn.) Urban Silicone Transdermal Patch for Wound Healing

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**Abstract**

This study aimed to develop silicone transdermal patches containing 0.5% w/w *Centella asiatica* (Linn.) Urban extract. Two types of transdermal patches were developed, a one-layer type and a two-layer type. The release of the extract from the patch was evaluated using Franz static diffusion cells. The amount of the active constituent of the extract released from the patch was determined in terms of the total phenolic content. Upon 16 hours of releasing, the total phenolic content was 0.61% for the one-layer type and 0.53% for the two-layer type of silicone patches. The adhesiveness of the patches was tested by a rolling ball tack tester. This test showed that the two-layer type was more adhesive than the one-type formulation. The “application satisfaction test” of the patches was performed on 10 normal volunteers. After applying the one-layer type, two-layer type and control type patches on the inside part of their forearms for at least 12 hours, the results showed that, in term of adhesiveness, the volunteers significantly preferred the one-layer type and the two-layer to control-type patches (p-value = 0.001 and 0.017, respectively). However, easy-peeling and overall preference scores of all patch types were not significantly different. These results could be used as a guideline for commercial product development of a centella silicone transdermal patch.

**Key words**: silicone transdermal patch, Centella asiatica (Linn.) Urban transdermal patch, soft skin adhesive

**Introduction**

A transdermal patch or skin patch is a medicated adhesive patch that is placed on the skin to deliver a specific dose of medication through the skin and into the bloodstream. Often, this method medication delivery promotes healing to an injured area of the body. One advantage of a transdermal drug delivery route over oral, topical application and others is that it provides a controlled release of the medication into the patient. A disadvantage to this development however, stems from the fact that the skin is a very effective barrier. A wide variety of pharmaceuticals can be delivered through transdermal patches.

Silicone dermal patch contains a soft skin adhesive gel. It combines with the self-adhering characteristics of silicone and with the cohesive properties of an elastomer matrix. These materials are useful in application over a scar wound that requires a soft material with adhesive properties. Researches have been shown that Pressure-Sensitive Adhesive was less adhesive and more force had to be applied to tear off the patch than that of silicone dermal patch (1,2). In this study, the *Centella asiatica* Silicone transdermal patch was developed for wound healing as a suitable adhesion and proper patch for patients.

**Materials and Experimental Procedures**

The different silicone dermal patches were prepared by mixing silicone polymers in different proportions, thus preparing 1 and 2 layer patches, degas before curing at 60°C, for 10 minutes then stickled with releasing membrane. The experiments were done in a controlled room at 25°C, 70% RH in order to provide the most preferred adhesive and stable patches. These patches were screened by thumb test before the addition of the *Centella asiatica* (Linn.) Urban extract.

**Evaluation of Silicone Transdermal Patches**

The release of bioactive components (as gallic acid) from the dermal patch was studied by using Franz static diffusion cells running at a temperature of 37°C over 16 hours. Tests for adhesiveness, irritation and adhesion satisfaction
Examination for Microbial Contamination in Silicone Transdermal Patches

Centella asiatica (Linn.) Urban silicone transdermal patches (Centella patch) were examined for microbial contamination in PCA (Plate count agar) where samples were incubated in media at 35°C for 24 hours.

Stability Testing of the Silicone Transdermal Patch

Centella patch and a controlled patch packed in the final packaging were kept at 4°C and at room temperature for 1 month. Accelerate stability tests were done by kept sample at 2°C and 45°C each of 24 hours for 7 cycles before the applied adhesive test.

Adhesive Test (Modified Rolling Ball Tack Tester)

All transdermal patches were tested for their relative adhesion in term of distance running when letting the stainless steel ball slide from a tangent aluminum tray above 22°C until the ball stop on the dermal patches which were laid at the end of the tray. The distances of the falling ball on the demal patches were measured relative to the different layers of patches.

Materials

Packaging materials and releasing liner were supplied by 3 M Industry, Thailand.

Silicone primer, silicone polymer and backing membrane, Thermal polyurethane (TPU) were purchased from Down Cunning Chemical, U.S Summit, the Centella asiatica (Linn.) Urban extract was purchased from Nadef Chemical Company.

Results and Discussion

Development of Controlled Transdermal Patch

Control patches could be produced at every size: 1x1 inch, thickness 0.3 cm., 3x3 inch, thickness 0.3 cm., 6x6 inch, thickness 0.3 cm and 6x12 inch, thickness 0.3 cm. They all had a smooth surface, a transparent, optical clarity and uniform thickness while staying flexible and soft.

Development of Centella Patch

The suitable concentration to provide medication in the silicone patch was 0.25% and 0.5% w/w with the sizes of the patches as 1x1 inch, thickness 0.3 cm and 3x3 inch, thickness 0.3 cm. in both types: single layer and double layers patches with the same feature as a control. The composition of the double layer and the single layer patch were not different. The adhesion of the single layer patch to the backing membrane was poor dues to the interference of the drug dispersed thoroughly in the patch. This problem was overcome by developing the double layer type.

Accelerate Stability Testing

The physical appearance of all patches remained unchanged.

Microbial Evaluation of Centella Patch

All patches would not allow microorganism to produce colonies with less than 102 cfu/g on PCA.

Adhesive Test

The most adhesive transdermal patch was the double layer patch compared to the single layer patch, and the least adhesive was the control. The distance of adhesion for the patches were 1.42 cm., 1.53 cm. and 1.98 cm. respectively.

Dissolution Test of Centella Patch by Franz Static Diffusion Cells

The single layer released the drug in higher percentage (0.61) than the doubled layers (0.53). (Figure 1)

This indicated that the drug in the single layer distributed more uniformly in the patch than that in the double layers in which the drug in the double layers might be diffused and adhered to the adjacent layer.
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Figure 1. Releasing of bioactive compounds of 0.5% Centella asiatica (Linn.) Urban extract (as gallic acid equivalence) from single and double layers silicone transdermal patch.

Satisfaction Test

The volunteers significantly preferred the one-layer type and the two-layer to controlled-type patches (p-value = 0.001 and 0.017, respectively). However, easy-peeling and overall preference scores of all patch types were not significantly different.

Conclusions

The 0.5% Centella asiatica (Linn) Urban silicone transdermal patches were prepared and tested as a medicated adhesive patch. The curing process should be improved in order to delivery a higher percentage of the extract to the skin. An in-vivo experiment should also be performed to demonstrate the delivery of a specific dose of medication through the skin and into the bloodstream.

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References

