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# Topical Hemostatic Effect of a Common Ornamental Plant, the Geraniaceae *Pelargonium zonale*

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*Geranium* has been traditionally used as a local hemostatic medicine in some Andean regions, but this effect has not been tested in controlled experiments. In the present report, the leaves of a geraniaceae (*Pelargonium zonale*) were tested on a bleeding rat model. The bleeding time was 50% shorter in the geranium leaf juice treatment group ( $18.10 \pm 2.03$  min) and 80% shorter in the geranium crushed-leaf group ( $7.10 \pm 0.88$  min) than in the control (nontreatment) group ( $37.6 \pm 3.04$  min),  $p < 0.0001$ . Bleeding time with guava (*Psidium guajava*) crushed leaves ( $39.90 \pm 1.54$  min) was not different from the control group. A proved hemostatic agent, gelatin sponge, had a similar effect as geranium juice ( $16.7 \pm 3.32$  min) in the same animal model. A buffer solution at pH 3 (the same pH as

the geranium leaf extract) did not have any hemostatic effect, and the bleeding time ( $39.3 \pm 2.71$  min) was not different from the control group. The dilution 1:4 geranium leaf juice at pH 3 ( $25.6 \pm 3.08$  min) or pH 5 ( $28.8 \pm 3.98$  min) still had a statistically significant hemostatic effect. The results confirm the hemostatic effect of *P. zonale* leaves and show that it is similar (geranium leaf juice) or better (crushed geranium leaves) than the hemostatic effect of a commercial hemostatic sponge. It seems that the hemostasis caused by *P. zonale* extract leaves is not due to its low pH. The potential benefits as a new, inexpensive, safe, and easily available natural topical hemostatic agent are discussed.

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**B**leeding can be the result of injury, blood disorders, or drug effect, and stopping hemorrhages very often demands an urgent crucial medical action. There are effective hemostatic drugs, such as antifibrinolytic amino acids (tranexanic acid and aminocaproic acid), aprotinin, and desmopressin. They are used in cardiac surgery, internal bleedings, or congenital bleeding disorders,<sup>1</sup> but they are not intended for local use. Topical hemostatic agents such as fibrin tissue adhesives, collagen, thrombin, and prothrombin are expensive and not easily available, and some of them have limited efficacy.<sup>1</sup> Therefore, effective topical agents are badly needed, not only for critical bleeding conditions but for common wounds or mucosa bleeding too.

There are many anecdotal references of curative uses of plants, but only some of them turn out to be true. Some natural substances have been traditionally con-

sidered effective to stop bleeding. To the best of our knowledge, only notoginseng, a Chinese root, has a well-documented local hemostatic effect.<sup>2,3</sup> Traditional oral references from the Andean people mention the benefits of geranium crushed leaves to stop bleeding on wounds or *epistaxis* (nasal bleeding) without conspicuous side effects. The common geranium, a popular ornamental and odorant plant, has some interesting biological and reported medicinal effects<sup>4-6</sup> that suggest that its use is at least nontoxic. However, there are no scientific references about its hemostatic effect. Our purpose was to study a geraniaceae, *Pelargonium zonale*, as a topical hemostatic agent in a rat model of external bleeding. The results suggest that geranium leaves could be an inexpensive, safe, and easy available topical hemostatic agent for skin or mucosa injuries.

## METHODS

### Plants

A plant popularly named geranium (*Pelargonium zonale* (L.) L'Her. ex. aiton) with hairy leaves, easily

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grown in home gardens, was used. This geranium was freshly prepared in a similar way that people traditionally do (i.e., manually crushing the leaves and directly applying them on wounds). Two clean and apparently healthy medium-size leaves weighing about 3 g were cut from the plant and crushed in a ceramic mortar for each experiment. The volume of the juice was about 1.5 mL, and the rest of the crushed wet material weighed about 1.5 g. The liquid or juice or the whole crushed material was immediately applied or stored at 4°C until used the same day, 1 hour later at the most. The juice was centrifuged at 3000 rpm  $\times$  6 min to obtain a supernatant that was collected in microvials and stored at 4°C for later use. Another plant with nonhemostatic effect, the guava or *Psidium guajava* L.,<sup>7</sup> was used as a control for the geranium effect. The guava leaves were prepared in the same way as the geranium leaves. The pH of the juice or supernatant of the crushed leaves of the plants was measured.

### Animal Preparation

This study was done following the Animal Care and Use Guide of our institution. Eighty male adult Wistar rats weighting 200 to 300 g, with unrestricted access to food and water, were used.

### Bleeding Animal Model

The animals were anesthetized with 100 mg/kg ketamine chlorhydrate intraperitoneally injected and placed in a prone position on a platform with their tails resting 10 cm below the surface. To standardize the degree of injury, the rat tail was transected at 0.5 cm from the tip. In these animals, the mean diameter of the tail tip was 2.5 mm, and the mean bleeding area was 4.9 mm<sup>2</sup>. The blood was blotted with filter paper until no blood was observed on the paper upon blotting. The time from the tail transection to the bleeding cessation was the bleeding time.<sup>2</sup>

### Experimental Groups

The animals were randomly assigned to one of eight groups of 10 rats each.

*Control or nontreatment group.* After tail transection, the tail tip was first blotted with filter paper. Then it was blotted every minute until bleeding cessation.

*Geranium leaf juice group.* After tail transection, the tail tip was first blotted with filter paper. Then it was in-

roduced for 2 minutes into a 200- $\mu$ L geranium juice microvial, without making any mechanical pressure against the tail tip.

*Geranium crushed leaf group.* After tail transection, the tail tip was blotted with filter paper. Then the surface of the transected tail tip was covered with a small amount of whole crushed leaves (juice and solid moiety) for 2 minutes. This amount was about 10 mg of wet crushed whole leaves to cover the bleeding surface of the wounded tail tip.

*Guava crushed leaf group.* To compare the potential mechanical effect of the whole crushed geranium leaves on tail hemostasis, crushed fresh guava leaves in the same amount as geranium were applied on the tip of the transected tail for 2 minutes.

*Gelatin sponges group.* To have a positive control group, we used a hemostatic topical agent made of porcine gelatin Gelfoam absorbable gelatin sponge (USP Pharmacia & Upjohn Co., Kalamazoo, MI). The whole wounded area was covered with a 5-mm<sup>2</sup> piece of sponge.

*pH 3 buffer solution group.* To have a pH control group similar to the geranium leaf juice group, we used as treatment a pH 3 buffer solution without geranium prepared with hydrochloric acid buffer. The following procedure was the same one as in the geranium leaf juice group.

*Geranium juice pH 3 and pH 5 groups.* To study the pH effect on the hemostatic action of the geranium, we prepared a geranium juice solution by diluting up to 1:4 of the pH 3 geranium juice with filtered distilled deionized water or diluting the geranium juice with phosphate buffer to obtain a pH 5 solution. Then we tested the hemostatic effect of these solutions in two groups of rats.

In all groups after the treatment, the tail tip was blotted with the filter paper every minute until bleeding cessation. After the completion of experiments, the animals were sacrificed with ketamine overdose.

### Standard Buffer Solutions

Hydrochloric acid buffer was prepared with 50 mL potassium chloride 0.2 M, 7.8 mL hydrochloric acid 0.2 M, and water up to 200 mL. Phosphate buffer was prepared with 50 mL monobasic potassium phosphate 0.2 M, 29.1 mL sodium hydroxide 0.2 M, and water up to 200 mL. The reagents were purchased from Sigma Co. (St. Louis, MO).

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**Statistical Analysis**

The bleeding times of the treated versus control group were compared using the one-way ANOVA test and the post hoc least significant difference Tukey-HSD test. The data were presented as mean  $\pm$  standard error mean. The significance level was set at  $p < 0.05$ .

**RESULTS**

The geranium juice and its supernatant after centrifugation had a lower pH than the guava leaves. Geranium pH was 3 and guava pH was 5. A drop of rat or human blood was immediately coagulated when mixed with 200  $\mu$ L of the geranium supernatant but not with guava juice.

The statistical analysis gave a significant difference among the five first groups,  $F(4, 45) = 38.43, p < 0.0001$ . There was a significant reduction of bleeding time in the animals treated with geranium compared with no treatment or guava leaves. The bleeding time was 50% shorter in the geranium juice group ( $p < 0.0001$ ) and 80% shorter in the geranium crushed leaves group when compared with control or guava groups ( $p < 0.001$ ) (Figure 1). The strongest hemostatic effect occurred in the crushed geranium leaves group. The blood loss was much lower (in the size of blood spots on the filter paper) in all the animals of this group. The bleeding stopped in just a few minutes in most of them ( $7.10 \pm 0.88$  min). The difference of the bleeding time in the mashed leaf group versus the juice group ( $18.10 \pm 2.03$  min) was statistically significant ( $p < 0.05$ ). Since this result could be attributed to a mechanical effect of the material as a compress on the bleeding surface, we compared the effects of the crushed geranium leaves versus the crushed guava leaves to investigate this possible explanation. The geranium crushed leaves group showed only 17.8% of the bleeding time of the guava group. The bleeding times of the guava group ( $39.90 \pm 1.54$  min) and the control group ( $37.60 \pm 3.04$  min) were not statistically different (ns). The positive control group with a hemostatic agent made of gelatin sponge had a shorter bleeding time ( $16.7 \pm 3.32$  min) compared with the nontreatment group, but it was not statistically different from the geranium juice group.

The results in Figure 2 show that the low pH alone did not have any hemostatic effect. The mean bleeding time in the pH 3 buffer solution group ( $39.3 \pm 2.71$  min) was similar to the control nontreatment group. The 1:4 diluted geranium solutions still had a hemostatic effect compared with the nongeranium solution. However, the bleeding times with the diluted geranium juice solutions were longer than with the concentrated gera-

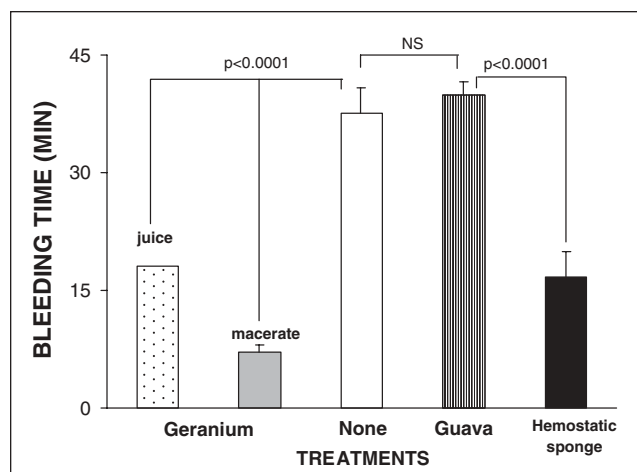


Figure 1. Geranium *Pelargonium zonale* leaves shorten the bleeding time in rats. The geranium (juice and crushed leaves) significantly reduced the bleeding time. The geranium crushed leaves had the greatest hemostatic effect. No differences were found between nontreatment and the guava crushed leaves. The gelatin sponge's hemostatic action was similar to the geranium juice.

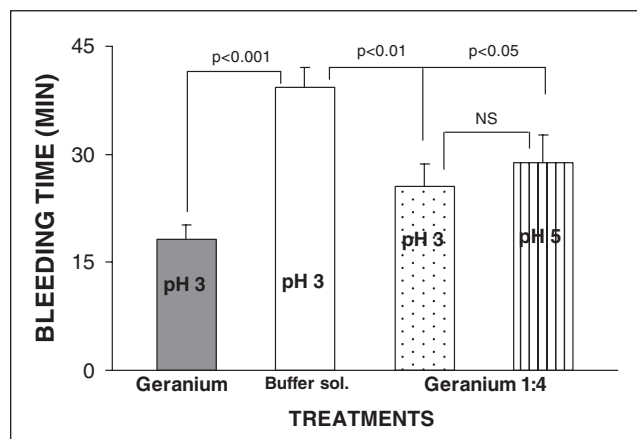


Figure 2. Low pH does not shorten the bleeding time in a rat model. The geranium leaves juice has a pH 3. A buffer solution at pH 3 without geranium did not have a demonstrable hemostatic effect. However, the 1:4 dilution of geranium juice in water at pH 3 or in phosphate buffer solution at pH 5 had the same hemostatic effect, although the bleeding time was longer than the pure geranium juice. This suggests that the acidic pH does not have much to do with the hemostatic effect of geranium leaves.

anium juice. There was no significant difference in the bleeding time between the diluted geranium solution group at pH 3 ( $25.6 \pm 3.08$  min) and at pH 5 ( $28.8 \pm 3.98$  min).

## DISCUSSION

The present simple experiments confirmed the efficacy of geranium leaves to shorten bleeding time in rats. The bleeding time was shortened 50% and 80% in the geranium juice and crushed leaves groups, respectively. Apparently, this effect is not due to a local mechanical action of the mashed leaves on the wound because the crushed leaves of the other plant, guava, had no effect on bleeding time. The positive control group with the gelatin sponge had a significant hemostatic action compared with the nontreatment group, and it was similar to the geranium juice effect. This commercial hemostatic agent used in dentistry is expensive and not so easy to find in poor countries. Nevertheless, it is more commonly used and less expensive than other hemostatic agents such as thrombin, prothrombin, and so on.

The results also show that the low pH of the plant was not a determinant in the hemostatic effect. Thus, the hemostatic effect itself and its apparent nontoxicity make the geranium a good prototype as a local hemostatic agent for testing in clinical situations.

Further research is needed to determine the mechanism of geranium hemostasis, the active substance or substances that facilitate coagulation or inhibit fibrinolysis, and the best method for extracting hemostatic compounds of the plant. Before trying the geranium for clinical uses, its toxicity needs to be tested, despite its successful use in infusions and topical applications. Since there is a demand for new natural hemostatic agents with potential uses in dental surgery, cardiovascular surgery, gastrointestinal bleeding, and bleeding in patients on anticoagulant or thrombolytic drugs, toxicity tests are warranted.

To our knowledge, no proven externally applied natural hemostatic agents have been reported in the medical literature, except the Chinese root notoginseng, which has been used as a hemostatic plant for centuries in China.<sup>2,3</sup>

The geranium, a common ornamental garden plant that is also used to extract perfumes, contains active substances with a variety of biological and pharmacological activities.<sup>4</sup> The tannin geraniin has an inhibitory effect on tumor necrosis factor (TNF) alpha release and an antioxidant effect with potential uses in cancer prevention.<sup>5,8</sup> The geraniin has a protective effect of gastric mucosa against ethanol damage,<sup>9</sup> and it seems to have an antihypertensive effect in rats.<sup>10</sup> The geranium also has antibacterial, fungicidal, and antiherpes virus action<sup>11,12</sup> and potential use in food processing.<sup>6</sup> An insect repellent effect and a radioprotective action also have been reported.<sup>13,14</sup>

The present report is the first in the medical literature about geraniaceae plants as a natural medicine for external bleeding, confirming what the oral tradition says.

In addition, the hemostatic plant extracts or their possible commercial derivatives could be more effective and cheaper than the topical hemostatic agents available at the present time.

## CONCLUSION

The geranium leaves (juice or crushed), applied externally, significantly shortened the bleeding time in a rat model. The positive control with the gelatin sponge, a well-known hemostatic agent, was similar to geranium juice in the bleeding model we used. This effect seems to be independent of the pH. Further research is needed to determine which active ingredients in the plant shorten bleeding time. This plant potentially could be used as a topical natural hemostatic agent that is probably nontoxic, cheap, and easily available.

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