The effects of *Aloe vera* [gel] on clotting time, prothrombin time and plasma fibrinogen concentration in albino Wistar rats

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Abstract

**Background:** Published reports on the effects of *Aloe vera* gel on blood coagulation in experimental animals are relatively scanty.

**Aim:** To determine the effect of *Aloe vera* gel on clotting time, prothrombin time and plasma fibrinogen concentration in albino Wistar rats.

**Methods:** A total of 28 adult albino Wistar rats divided into 4 groups (Groups 1, 2, 3 and 4) consisting of 7 rats in each group were used for the study. Groups 1, 2 and 3 served as the experimental groups, while Group 4 rats served as control. Rats in Groups 1, 2 and 3 were given respectively 200mg/kg/day, 100mg/kg/day and 50mg/kg/day of the *Aloe vera* gel on alternative days for 14 days. Rats in Group 4 [control] were given 1ml of distilled water in a similar manner. All the doses were given intra-peritoneal. The gel was obtained from the transparent mucilage of the leaves of the *Aloe vera* plant. Blood samples were obtained from the rats by direct cardiac puncture under chloroform anaesthesia. Prothrombin time was determined using 0.0325M calcium chloride and commercial thromboplastin; clotting time was determined using the Lee-White method as both the intrinsic and extrinsic pathways. Plasma fibrinogen concentration was determined by the clot weight method as described by Ingram (1961).

**Results:** Results obtained indicate that treatment with the *Aloe vera* gel significantly prolonged (p<0.05) in a dose dependent manner the prothrombin time in Groups 1 and 2 rats: with values of 15.00±1.00 seconds and 13.00±0.82 seconds respectively, compared to the control group value of 7.30±1.52 seconds. Similarly, treatment with the *Aloe vera* gel significantly prolonged (p<0.05) in a dose dependent manner the clotting time in all experimental rat groups. The value of the clotting time in control group was found to be 213±20.80 seconds. Treatment with *Aloe vera* extract prolonged the clotting time in Groups 3, 2 and 1 to values of 222±21.60 seconds, 327±34.03 seconds and 356±15.20 seconds respectively. In addition, treatment with *Aloe vera* was found to significantly decrease (p<0.05) the plasma fibrinogen concentration in a similar dose dependent manner. The values for Groups 1 and 2 were found to be 80.0 ±10.0 g/dl and 97.5 ±9.57 g/dl respectively, both values were found to be significantly higher (p<0.05) than the value obtained for the control rats which was 21.3 ±5.78 g/dl.

**Conclusion:** The present study suggests that *Aloe vera* gel could inhibit blood clotting via actions on both the intrinsic and extrinsic pathways. Further studies are however recommended in this regard.

**Key words:** Aloe vera, Clotting time, Plasma fibrinogen concentration, Prothrombin time

Introduction

*Aloe vera* is a stem-less or very short-stemmed succulent plant of the Asphodelaceae family. Its green leaves are lanceolate, thick and fleshy with serrated margins. The plant is native to North Africa, but is cultivated in the drier tropic and sub-tropic regions of the world as an ornamental and medicinal plant. *Aloe vera* can be separated into two basic products: gel and latex. Aloe gel is the transparent mucilage obtained from the pulp of the leaves. Aloe latex [juice] is the bitter yellow exudate
obtained from the outer skin of the leaves. Traditional medicinal uses also differ. Whereas aloe gel is used for topical treatment of wounds, minor burns and a variety of skin conditions, aloe juice is commonly used as an oral laxative and cathartic.

Several scientific reports have attempted to provide valid supporting evidence for the anecdotal effects and folklore uses of Aloe vera. The numerous and varied constituents of Aloe vera have contributed to its multi-faceted use, abilities and applications. In addition, although several studies have indicated a beneficial effect of Aloe vera in the healing of wounds and burns; scientific reports of the effects of Aloe vera gel on blood coagulation and plasma fibrinogen concentration are relatively scanty. However, an anti-angiogenic effect has been described which could expectedly lead to impaired wound healing. The objective of the present study was to determine the effect of Aloe vera gel on prothrombin time, clotting time, and the plasma fibrinogen concentration of albino Wistar rats. This is to further characterize the effects of Aloe vera on blood clotting.

Material and Methods

A total of 28 Wistar rats were used for the study. Prior to experimentation all the animals were allowed four weeks to acclimatize to their environment during which period they all had free access to tap water and rat feed ad libitum (Pfizer Nigeria Plc).

Aloe vera plant was obtained from the environment of the University of Port Harcourt, Nigeria. The fresh leaves were then thoroughly washed with clean tap water to remove dirt. The base and apex of the leaves were cut with surgical blades and the margins also sliced off carefully. A slice was made through the cut margins of the Aloe vera leaf to reveal the transparent mucilage. With the aid of a spatula the transparent mucilage was carefully removed into a beaker and further processed by blending in an electric blender for 20 minutes. A greenish but gel-like liquid was obtained. This was then allowed to settle in the laboratory for 20 minutes. The liquid was gently sieved in Whartman filter paper one to harvest a particulate-free filtrate. Thirty milliliters of distilled water was next added to 4.79g of the extracted Aloe vera gel to give an extract concentration of 159.7mg/ml.

The rats were then divided into four experimental groups: 1, 2, 3 and 4 consisting of 7 rats each; group 4 served as the control arm. All rats in experimental Group 1 were given extract doses of 200mg/kg/day; Group 2 was given extract doses of 100mg/kg/day and rats in experimental Group 3 were given 50mg/kg/day. The extracts were given on alternate days for 14 days. The rats of the control (Group 4) were given 1ml of normal saline in a similar alternate day sequence. All doses were given intra-peritoneal.

On day 15, the rats were anaesthetized with chloroform and dissected to expose their thoracic cavity and hearts. Blood was thus obtained by careful cardiac puncture. A portion of the collected blood was immediately transferred into sample bottles containing 3.8% sodium citrate in the ratio of 9:1 to enable determination of prothrombin time and plasma fibrinogen concentration.

The following parameters were determined: clotting time, one stage prothrombin time and plasma fibrinogen concentration. Clotting time was determined using the Lee-White method as described by Ochei and Kolhatkar (2000). One stage prothrombin time was determined using 0.025M calcium chloride and commercial thromboplastin as described by Ochei and Kolhatkar (2000). Plasma fibrinogen concentration was determined by the clot weight method as described by Ingram (1961). Results obtained are as presented in tables. Means and standard deviations were calculated. Statistical differences were determined using the students’ t-test. A p value less than 0.05 was considered statistically significant.

Results

Table 1 shows the effect of Aloe vera extract on prothrombin time. The prothrombin time of control rats was found to be 7.30±1.52 seconds. Treatment with Aloe vera prolonged the prothrombin time in a dose dependent manner in
all treatment groups. For Groups 1 and 2 rats, treatment with Aloe vera extract for two weeks prolonged the prothrombin time to values of 15.00±1.00 seconds and 13.00±0.82 seconds respectively; both values were found to be significantly higher than the value of the control group (p<0.05). There was a non-significant increase in the prothrombin time of Group 3 rats to a value of 10.75±0.95 seconds.

**Table 1. The effect of Aloe vera gel on prothrombin time**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Doses [mg/kg/day]</th>
<th>Prothrombin time (Seconds)</th>
<th>Significant differences [t-test]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 4:</td>
<td>1 ml of normal saline</td>
<td>7.30±1.520</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>200mg/kg</td>
<td>15.00±1.000</td>
<td>Yes [p&lt;0.05]</td>
</tr>
<tr>
<td>Group 2</td>
<td>100mg/kg</td>
<td>13.00±0.816</td>
<td>Yes [p&lt;0.05]</td>
</tr>
<tr>
<td>Group 3</td>
<td>50mg/kg</td>
<td>10.75±0.957</td>
<td>No [p&gt;0.05]</td>
</tr>
</tbody>
</table>

**Table 2. The effect of Aloe vera gel on clotting time**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Doses [mg/kg/day]</th>
<th>Clotting time (Seconds)</th>
<th>Significant differences [t-test]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 4:</td>
<td>1 ml of normal saline</td>
<td>213±20.80</td>
<td></td>
</tr>
<tr>
<td>Control group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>200mg/kg</td>
<td>356±15.20</td>
<td>Yes [p&lt;0.05]</td>
</tr>
<tr>
<td>Group 2</td>
<td>100mg/kg</td>
<td>327±34.03</td>
<td>Yes [p&lt;0.05]</td>
</tr>
<tr>
<td>Group 3</td>
<td>50mg/kg</td>
<td>220±21.60</td>
<td>Yes [p&lt;0.05]</td>
</tr>
</tbody>
</table>

Table 2 shows the effect of Aloe vera extract on clotting time. Similarly, treatment with Aloe vera extract was found to prolong clotting time significantly and in a dose dependent manner. The value of the clotting time in control group was found to be 213±20.80 seconds; treatment with Aloe vera extract prolonged clotting time in Groups 3, 2 and 1 to values of 222±21.60 seconds, 327±34.03 seconds and 356±15.2 seconds respectively. All values were found to be significantly higher than the control values (p<0.05).

Table 3 shows the effect of Aloe vera extract on the plasma fibrinogen concentration. The value of plasma fibrinogen concentration in the control group was found to be 213±5.78 g/dl. Treatment with Aloe vera extract decreased plasma fibrinogen concentration in a dose-dependent manner. The values for Groups 1 and 2 were found to be 80.0±10.0 g/dl and 97.5±9.57 g/dl respectively. Both values were significantly lower than the value obtained for the control rats (p<0.05). There was a non-significant decrease in the plasma fibrinogen concentration of Group 3 rats to a value of 162.5±17.07 g/dl.

**Discussion**

Unexpectedly, the result obtained in the present study suggests that Aloe vera gel could inhibit blood coagulation via a significant and dose dependent increase in prothrombin time and clotting time and decrease in plasma fibrinogen concentration in
albino Wistar rats. These indices are measures of blood coagulation. While the clotting time measures the intrinsic pathway, the prothrombin time measures the extrinsic pathway of blood coagulation. Fibrinogen concentration is critical to the formation of a stable fibrin clot. In addition, whereas the clotting time indicates the functions of clotting factors I, II, V, VIII, IX, X, XI and XII, the prothrombin time indicates the functions of factors II, V, VII X and fibrinogen. Previous studies on the effects of Aloe vera on blood clotting in experimental animals are relatively scanty.

Although, precise mechanisms of action of Aloe vera gel of inhibiting blood coagulation are at present uncertain. Aloe vera has been reported to enhance pain management by inhibiting the production of bradykinin and thromboxane and to improve blood circulation via a vasodilator effect. In addition, it has been reported to possess immune-stimulatory, anti-bacterial, anti-fungal, anti-viral and anti-oxidant activities. Anti-inflammatory actions by an inhibitory action on the arachidonic acid pathway via cyclooxygenase have also been described. Other studies have reported an anti-diabetic, anti-ulcer, and anti-cancer activities. A recent review suggests Aloe vera to be effective in reducing both blood glucose and lipid levels in patients with diabetes and hyperlipidaemia. A similar effect has been shown in streptozotocin-induced diabetic rats.

Overall, it is at present unclear how the reported effects of Aloe vera above and its inhibition of blood coagulation described in the present study could contribute to its effect in improving the wound healing process. Most studies describe its healing effects on wound and burns by several diverse mechanisms including enhancing early epithelization of burn wounds; enhancing the production of a wound-healing advancement factor; acting as an antibacterial agent; enhancing the collagen matrix of wounds; and causing an increase in capillary blood flow amongst other mechanisms.

In conclusion, the present study reports that Aloe vera gel significantly increased prothrombin time and clotting time and reduces plasma fibrinogen concentration in albino Wistar rats. The significance of these findings in light of the established wound healing actions of Aloe vera gel is unclear. We recommend further studies to in this regard.

References


