



Alteration Of Procoagulant Activity Of Hemocoagulase By Herbal Drugs

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ABSTRACT:

Hemocoagulase drug is widely used as an effective procoagulant during surgical procedures. It prevents excessive blood loss during surgeries by accelerating the hemostasis process. Herbal drugs/medicinal plants have the potential to alter the desired medicinal properties of synthetic and isolated drugs. To study the effect of herbal drugs on the procoagulant activity of hemocoagulase, eighteen medicinal plants were tested to detect potential interference in the functioning of hemocoagulase as a hemostatic agent. Whole blood clotting time of drug-plant ext. was measured, *in vitro*. *Glycyrrhiza glabra* and *Alium sativium* were found to affect the procoagulant activity of hemocoagulase. Hence, it is recommended to check the history of consumption of herbal drugs by the patients before doing any major surgery, specifically, tooth extraction surgery, wherein, hemocoagulase is routinely used as a hemostatic drug.

KEYWORDS: Procoagulant, clotting time, hemocoagulase, drug interactions, hemostasis

INTRODUCTION:

Post-operative blood loss is a major concern for surgeons. In some cases, post-traumatic bleeding can be life-threatening (1). The drug Hemocoagulase is widely used as an effective procoagulant during surgical procedures. The enzyme hemocoagulase is fractionated from Bothrops venom (2, 3). It exhibits thrombin-like action in the coagulation process (4). It was found to be effective in reducing postoperative bleeding (5-11) as well as in the blood transfusion step during cardiac surgeries (12). It was found to be useful in the prevention of post-biopsy bleeding (13). Hemocoagulase was also found to be effective in the reduction of the volumes of hemorrhagic blood (14). It is preferentially used in dental surgeries, specifically, to accelerate wound healing of the socket site after tooth extraction (15-17).

Herbal drugs/medicinal plant parts have a wide range of biological activities. Most of the time, herbal drugs are consumed by patients along with prescription drugs without considering any potential drug interactions. Some medicinal plant parts/extracts may interact with the prescription drugs which may result, either in the enhancement of the desired medicinal properties, or may decrease the efficacy of prescription drugs (18-23). This may lead to complications during or after operative treatments.

The present study aims to investigate possible interactions of some selected medicinal plant extracts with hemocoagulase which would help healthcare providers in taking necessary precautions before any invasive treatment.

MATERIALS AND METHODS:

Sixteen medicinal plant parts were obtained from herbal medical practitioners (two were obtained from local markets- *Allium sativum* and *Embilica officinalis*). The plant parts were ground to obtain in powder form. Sterile saline solution of 9% NaCl was used to prepare aq. extracts. All the plant extracts were prepared in saline solution and ethanol (1: 5 w/v). Human whole blood was used to test clotting time (without separation of plasma). Trisodium citrate solution (3.8%) was added to whole blood (1:9 v/v) to cease the coagulation process (24, 25). Hemocoagulase sterile solution (0.2CU) was mixed with each ext. (1:1 v/v). The control (blank) was prepared by mixing hemocoagulase (Hc) and saline solution (1:1 v/v). Citrated blood (100 µl) was added into each Hc + plant ext. mixture. 100 µl CaCl₂ solution (0.025 moles/L) was added to the Hc + ext. + blood mixture to initiate the coagulation process. Whole blood clotting time was measured by using Lee and White method. The extracts that were found to interact with Hc were heated up to boiling and were further tested using the same method.

RESULTS AND DISCUSSION:

The control (Hc + Saline solution) was clotted after 5.30 min. Out of eighteen aq. extracts of medicinal plants; seventeen aq. extracts were also clotted within the same time period, which indicates no drug-herb interactions (table 1.1).

Table 1.1: Clotting Test (aq. ext.)

Drug + Plant Ext.	Plant Part Used	Clotting Test
Hc + <i>Withania somnifera</i>	Root	C
Hc + <i>Adhatoda vasica</i>	Leaves	C
Hc + <i>Curcuma amada</i>	Rhizome	C
Hc + <i>Embilica officinalis</i>	Fruit	C
Hc + <i>Hemidesmus indicus</i>	Root	C
Hc + <i>Terminadia arjuna</i>	Bark	C
Hc + <i>Acacia Arabica</i>	bark	C
Hc + <i>Mimusops elengi</i>	Bark	C
Hc + <i>Psoralea corylifolia</i>	Seed	C
Hc + <i>Terminalia chebula</i>	Fruit	C
Hc + <i>Nardostachys jatamansi</i>	Rhizome	C
Hc + <i>Allium sativum</i>	Bulb	C
Hc + <i>Curcuma zedoaria</i>	Rhizome	C
Hc + <i>Rubia cordifolia</i>	Stem	C
Hc + <i>Acacia catechu</i>	Stem	C
Hc + <i>Glycyrrhiza glabra</i>	Root	N
Hc + <i>Alpinia galanga</i>	Root	C
Hc + <i>Picrorhiza kurroa</i>	Rhizome	C
Hc + Saline solution (Control)	--	C

(Hc: Hemocoagulase, C: Clotted, N: Not Clotted)

Hc + *Glycyrrhiza glabra* mixture did not clot for a prolonged time period; which indicates loss of procoagulant activity of Hc in the presence of *Glycyrrhiza glabra* (Table 1.1).

Ethanol ext. of sixteen plants were clotted along with control with same time period, i.e., around 5.30 min. The ethanol ext. of two plants (*Glycyrrhiza glabra* and *Allium sativum*) pronged the clotting process (table 1.2). This suggests that the aq. ext. of *Allium sativum* has no effect on the functioning of Hc as hemostatic agent but its ethanol ext. has the potential to destroy its procoagulant activity.

Table 1.2: Clotting Test (ethanol ext.)

Drug + Plant Ext.	Clotting Test
Hc + <i>Withania somnifera</i>	C
Hc + <i>Adhatoda vasica</i>	C
Hc + <i>Curcuma amada</i>	C
Hc + <i>Embilica officinalis</i>	C
Hc + <i>Hemidesmus indicus</i>	C
Hc + <i>Terminadia arjuna</i>	C
Hc + <i>Acacia Arabica</i>	C
Hc + <i>Mimusops elengi</i>	C
Hc + <i>Psoralea corylifolia</i>	C
Hc + <i>Terminalia chebula</i>	C
Hc + <i>Nardostachys jatamansi</i>	C
Hc + <i>Allium sativum</i>	N
Hc + <i>Curcuma zedoaria</i>	C
Hc + <i>Momordica charantia</i>	C
Hc + <i>Acacia catechu</i>	C
Hc + <i>Glycyrrhiza glabra</i>	N
Hc + <i>Alpinia galanga</i>	C
Hc + <i>Picrorhiza kurroa</i>	C
Hc + Ethanol (Control)	C

The boiled ext. of *Glycyrrhiza glabra* prepared in both the solvents prolonged the clotting process (table 2.1); this indicates that *Glycyrrhiza glabra* retains its ability to alter the hemostatic process even after boiling.

Table 2.1: Aq. ext. (boiled)

Drug + Plant Ext.	Clotting Test
Hc + <i>Glycyrrhiza glabra</i>	N
Hc + Saline solution (Control)	C

Table 2.2: Ethanol ext. (boiled)

Drug + Plant Ext.	Clotting Test
Hc + <i>Allium sativum</i>	C
Hc + <i>Glycyrrhiza glabra</i>	N
Hc + Ethanol (Control)	C

The ethanol ext. of *Allium sativum* (without any heat treatment) prolonged the clotting time, but its boiled ext. did not show the same effect (table 2.2).

CONCLUSION:

The two plants, *Glycyrrhiza glabra* and *Allium sativum* have the potential to interfere with the procoagulant activity of hemocoagulase. In the case of *Glycyrrhiza glabra*, both aq. and ethanol extracts vanished the procoagulant activity of hemocoagulase. Only the ethanol ext. of *Allium sativum* destroyed the procoagulant activity. There was no effect of its aq. ext. on the clotting process. This could be a concern for a majority of patients who consume liquor because of the ethanol content in any form of liquor. The biologically active molecules present in *Allium sativum* may dissolve to a larger extent in the ethanol-containing liquor and may get easily absorbed in the intestinal part of the digestive tract. This may complicate further if *Allium sativum* is consumed in raw form. It would be better to know the history of consumption of herbal drugs/alternative medicines by the patients before using haemocoagulase for the treatment of bleeding

tendency, or, before doing any surgery, wherein, excessive blood loss is expected. These results are obtained through *in vitro* experiments; therefore, it is recommended to do further research, *in vivo* and to test other commonly used herbal drugs and synthetic procoagulant drugs.

CONFLICT OF INTEREST:

The authors have no conflicts of interest regarding this investigation.

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