Adjunctive hemostatic application of highly adhesive drug loadable powder for partial hepatectomy bleeding in a swine model

Eunhye Lee*, Sukyung Ahn*, Yonghai Nam*, Keunsu Kim*, Don Haeng Lee Don Haeng Lee*, **

* Utah-Inha DDS and Advanced Therapeutics Research Center, Incheon, Republic of Korea

** Division of Gastroenterology, Department of Internal Medicine, Inha University hospital, Incheon, Republic of Korea

BACKGROUND & AIM

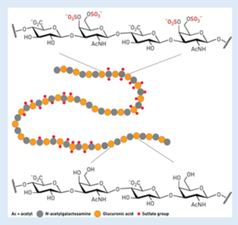
Topical agents can be effective as adjuncts to aid in hemostasis when bleeding is not controllable with general methods. Such adjunctive hemostatic treatments include topical gelatins, collagens, thrombin and fibrin sealants, synthetic glues, and glutaraldehyde-based glues. UI-SAH is a highly adhesive drug-loadable powder that has been developed for adjunctive hemostatic use. The hemostatic effects are achieved by forming a hydrogel and showing high adhesiveness and biodegradation on bleeding site. And besides, amine containing therapeutic molecules such as vancomycin, mitomycin, and gemcitabine can be easily loaded into UI-SAH without chemical modification.

The aims of this study were to confirm 1) the effectiveness of the application of UI-SAH powder in hepatectomy bleeding swine model, 2) the prevention of organ adhesion after gelation at the bleeding site and 3) the feasibility of the drug loading capacity.

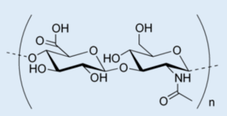
MATERIALS & MECHANISM

Materials

Oxidized glycosaminoglycan (GAG)

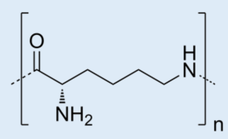


Chondroitin sulfate

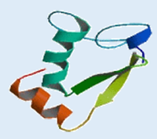


Hyaluronic acid

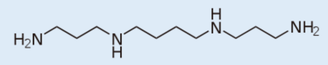
Modified Polyamine



Poly-L-lysine

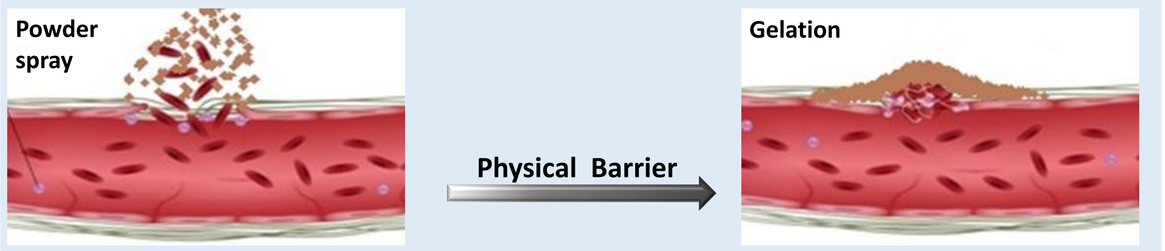


Protamine



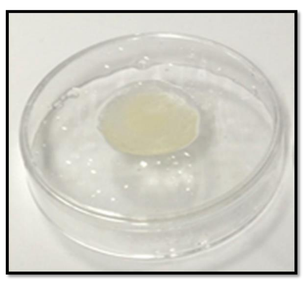
Spermine

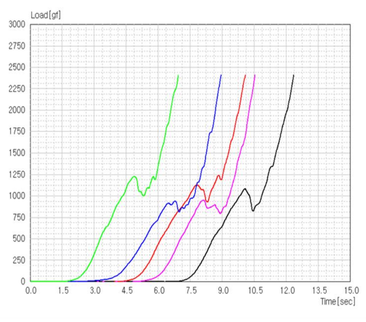
Mechanism



METHODS & RESULTS

1. Physical properties of UI-SAH





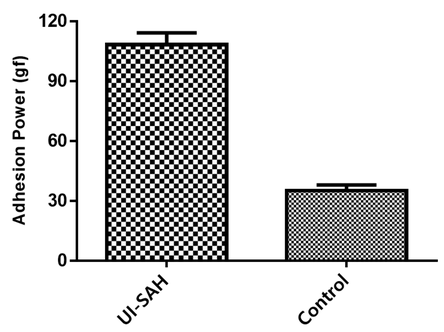
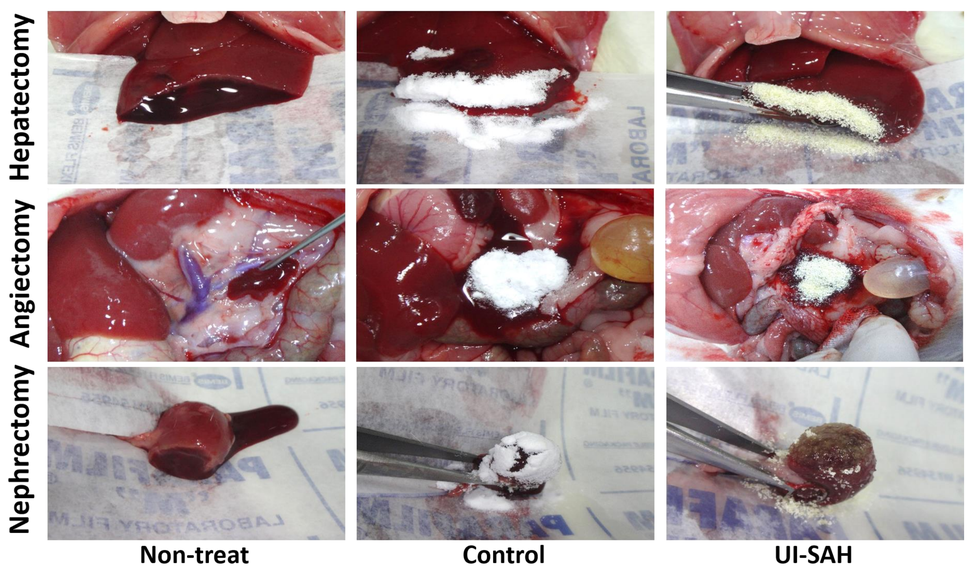


Figure 1. UI-SAH Gel morphology and gel strength after gelation

Gel strength and adhesion forces of UI-SAH gel were measured by TXA™ Texture Analyzer (Yeonjin Corporation, Seoul, South Korea). UI-SAH was converted into adhesive gel after contacting water or blood within 20 sec, gel strength was 0.133 Mpa, Adhesion force was over 100 gf.

2. *In vivo* hemostatic effects (Rat bleeding model)



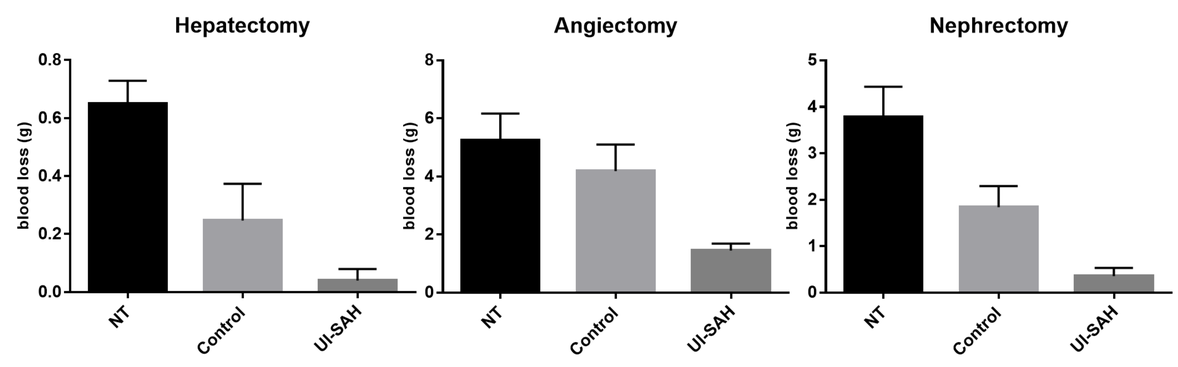
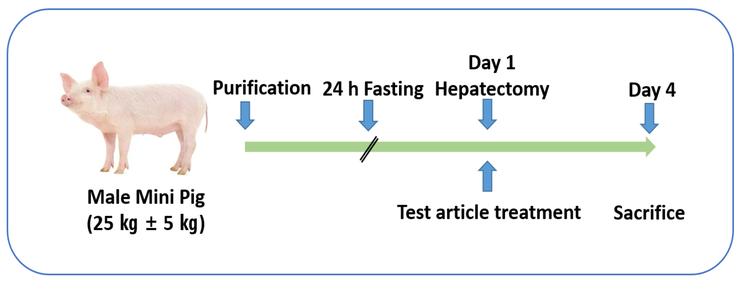
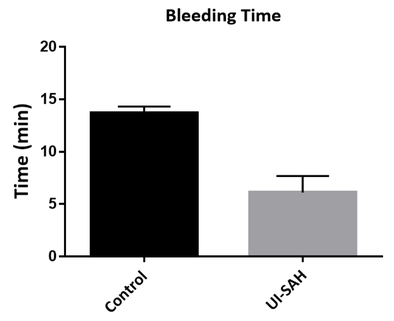


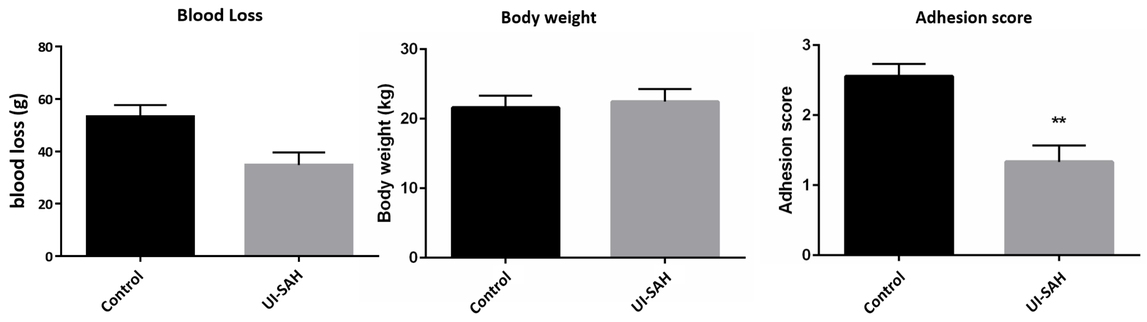
Figure 2. Evaluation of *in vivo* hemostatic ability in Rat bleeding model

To investigate the hemostatic ability of the UI-SAH, partial hepatectomy model, a vascular injury model, and a renal resection model were prepared and the blood loss was measured. UI-SAH significantly reduced bleeding compared to the control group.

3. *In vivo* hemostatic effects (Porcine hepatectomy model)







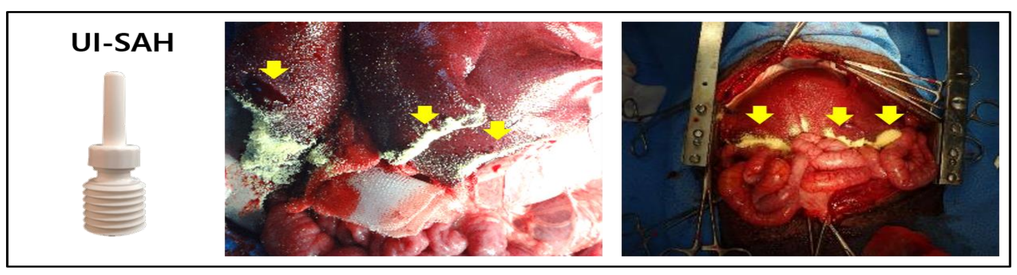


Figure 3. Evaluation of *in vivo* hemostatic ability in partially hepatectomized pigs

Mini-pigs underwent left partial hepatectomy and the UI-SAH was applied to the resection margin. Blood loss was measured at the time of exposing the resection margin after the confirmation of hemostasis.

4. *In vivo* drug loadable efficacy test (Orthotopic breast cancer model)

No.	Group	Name	Drug	PTX dose (mg/kg)	Administration route
1	Non-Treat	NT	-	-	-
2	Negative control	SAH	SAH	-	s.c. insertion
3	Test	SP	SAH + Paclitaxel	60	s.c. insertion
4	Positive control	PTX	Paclitaxel	60	IT

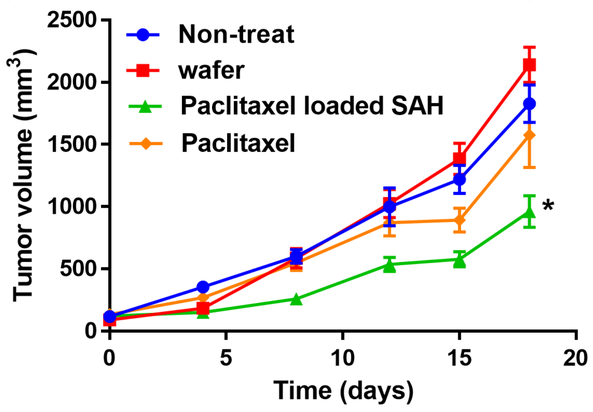


Figure 4. Evaluation of *in vivo* drug loadable efficacy in orthotopic breast cancer mouse model

In a tumor bearing mice model, the tumor volume of anti-cancer drug-loaded UI-SAH group was significantly decreased approximately 50% compared with those of positive control group on day 35 after tumor inoculation.

CONCLUSION

This study confirmed that the adjunctive hemostatic application of UI-SAH is effective for the in partial hepatectomy bleeding model due to high adhesiveness and the suppression of organ adhesion. Furthermore, tumor suppression can be accelerated by loading of the anti-cancer drug in the UI-SAH. The present study suggests that UI-SAH is promising candidate for adjunctive surgical hemostasis and local anti-cancer therapy.

ACKNOWLEDGEMENT

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