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# Removal of DOACs from plasma: performance comparison and pre-analytical considerations of three different devices

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## Introduction

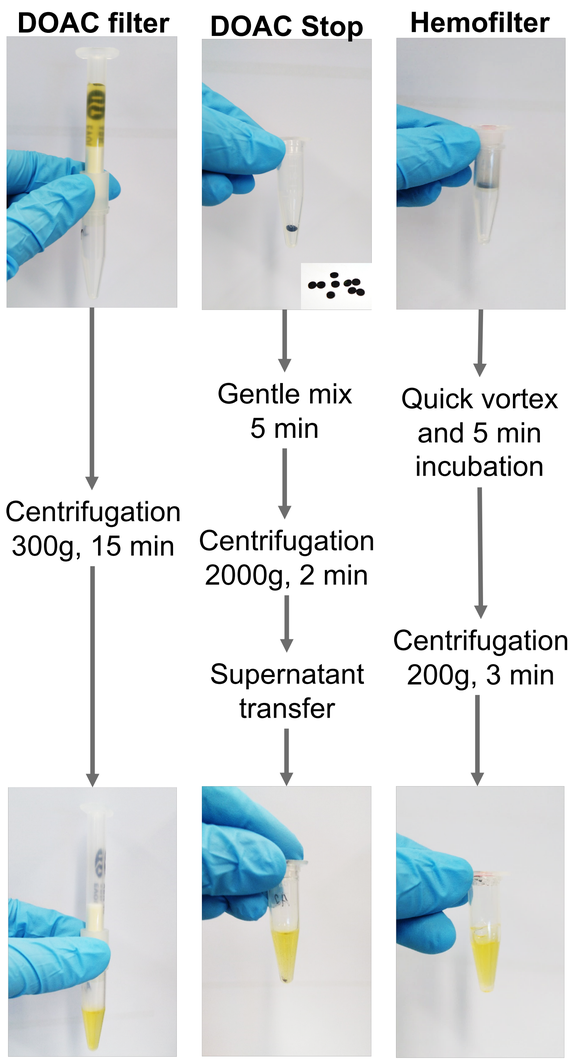
Given the plethora of coagulation tests influenced by Direct Oral Anti-Coagulants (DOACs), it would be of particular interest to **remove DOACs from a sample**. This could enable a better investigation of an underlying plasma defect potentially hidden by a **DOAC interference**. In this context, several **DOACs-removal devices** have been developed for a potential use in **clinical routine**. The transfer of plasma through a filter or the addition of an adsorbing agent is currently under investigation.

The aim of this study was to evaluate the performances of **three devices enabling the removal of DOACs** from spiked plasma samples. Their efficiency to eliminate DOACs from plasma, the impact of the transfer through the filters on the coagulation and their ergonomics were investigated.

## Methods

Fresh normal pooled plasma from 6 healthy volunteers were mixed with either **dabigatran, rivaroxaban or apixaban** at 0-125-250-500 ng/mL theoretical final concentration. Six hundred µL of plasma were tested before and after filtration on **DOAC filter** (Stago, France), **DOAC Stop** (Haematex Research, Australia) or on **Hemofilter** (Hemosafe, Belgium) on a STA-R Max2 analyzer using calibrated STA-Liquid anti-Xa or STA-ECAII for **dosage of anti-Xa and anti-IIa drugs**, respectively (all products from Stago, France). Prothrombin time (**PT**) and activated partial thromboplastin time (**aPTT**) were also analyzed on the STA-R Max2. Several **usage data** regarding these devices were collected throughout the study.

## 1- Procedure for DOAC removal

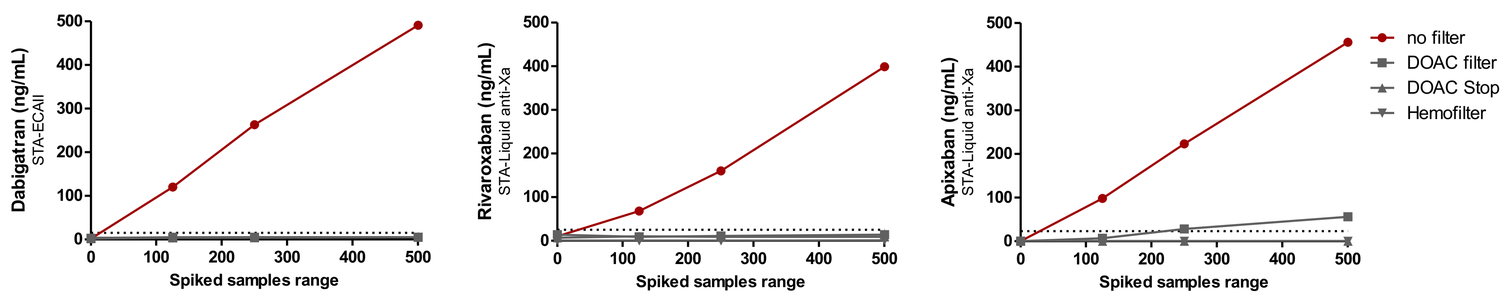



| Total time for use | | |
|---|---|---|
| 15 min | 7 min | 8 min |
| **Plasma volume loss** | | |
| 100±13 µL | 150 µL* | 68±3 µL |

*defined in the experimental design.

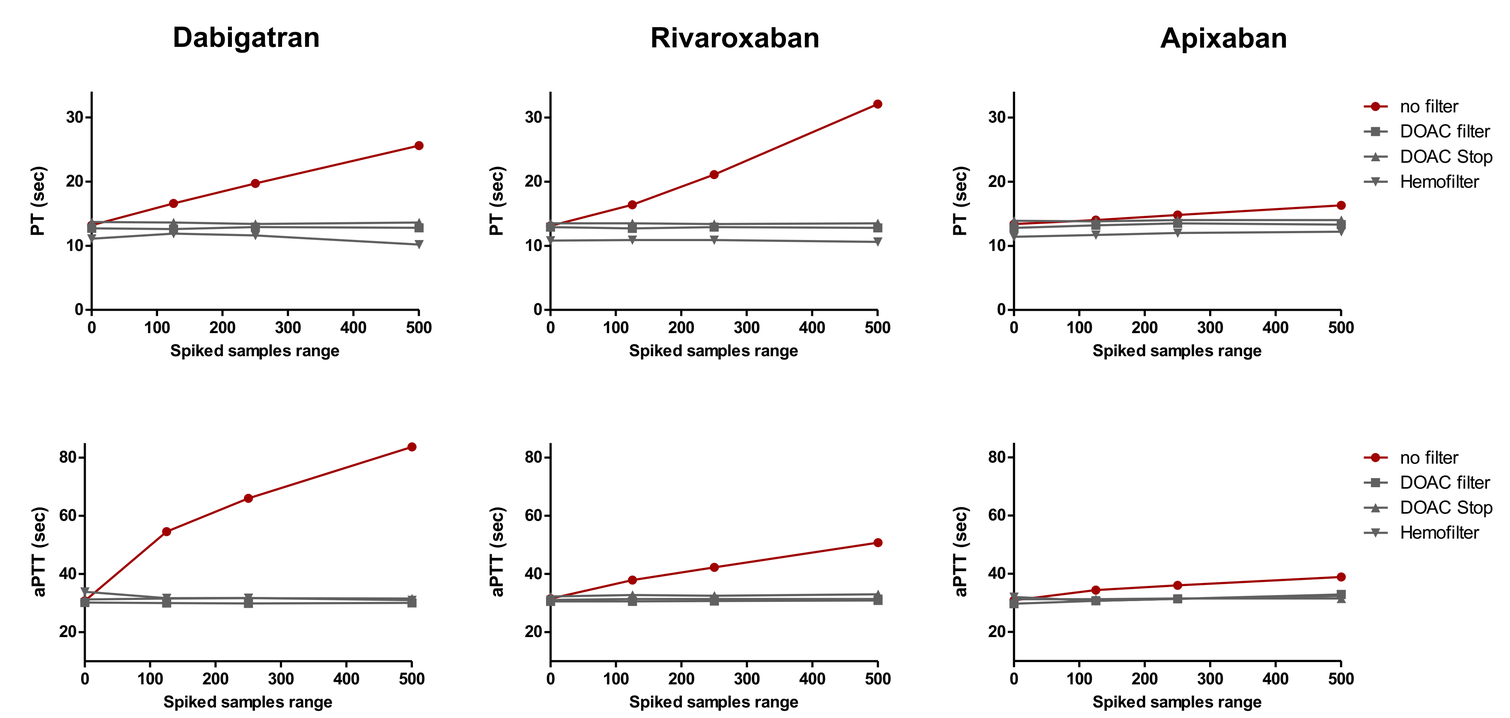
Regarding their ergonomics and usage data, the **DOAC Stop procedure is the quickest** (7 min). However, the complete elimination of the adsorbing agent is difficult and black residues in the sample were still visible after the procedure and **may lead to inadvertent transfer of the black residue which will re-introduce the DOAC into the sample**. The use of DOAC filter and Hemofilter include less steps in their protocol. The **Hemofilter induces the lower loss of sample volume**.

## 2- DOAC removal efficiency




Some discrepancies can be observed between theoretical and actual dosages of dabigatran, rivaroxaban and apixaban in spiked samples. Results also show that all devices enable a sufficient removal of rivaroxaban and dabigatran to lower measurements under the limits of detection of the instrument (LOD is presented as horizontal dotted line). For apixaban, only the DOAC Stop and the Hemofilter enable this sufficient elimination while residual amounts of apixaban are still measurable after the use of the DOAC filter on samples containing the highest concentrations tested (250 and 500 ng/mL theoretical).

## 3- Impact on PT and aPTT




All the DOACs-removal devices were able to restore normal PT and aPTT, but Hemofilter introduced a slight shortening of PT under every condition while it has no impact on aPTT.

## Conclusion

In conclusion, the DOAC Filter and the Hemofilter are the easiest DOAC removal devices to use. In addition, no visible residues potentially interfering with measurement are observed with these devices as opposed to DOAC Stop. However, the DOAC Filter is not able to eliminate apixaban at concentration higher than 250 ng/mL.

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