

# Interaction of direct oral anticoagulants and other anticoagulants in DOAC Dipstick tests

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## INTRODUCTION

Determination of direct oral anticoagulants (DOACs) in the presence of other anticoagulants (ACs) by conventional coagulation assays remains a major challenge in emergency care. In vitro neutralization of ACs improves the validity of coagulation assays but limitations still remain. The DOAC Dipstick sensitively and specifically detects the direct oral thrombin inhibitor dabigatran (DTI) and direct oral factor Xa inhibitors (DXI) in urine.

## AIM

To investigate the interaction of DTI and DXI with unfractionated heparin (UFH), low-molecular molecular weight heparin (LMWH), fondaparinux, r-hirudin and argatroban.

## CONCLUSIONS

- 1) DOACs do not interact with different AC heparin classes in urine on factor Xa and thrombin inhibitor pads.
- 2) At high concentrations, other DTIs are detected in urine by the DOAC Dipstick on thrombin inhibitor pad.
- 3) Determination of DOACs in urine with DOAC Dipstick does not interact with other ACs in patients treated with DOACs.

## RESULTS

Factor Xa (FXA, fig. 1) and thrombin inhibitor (THR, fig. 3) pads were all negative in the absence or presence of UFH, LMWH nadroparin, enoxaparin and fondaparinux. The positivity of all FXA pads of patients treated with apixaban was not affected by spiking of samples with UFH, LMWH and fondaparinux (fig. 2). THR pads were positive only in the presence of high concentrations of r-hirudin (1 µg/ml, fig. 3) and argatroban (6 µg/mL, not shown). The positivity of the THR pads of patients treated with dabigatran did not change when spiked with other thrombin inhibitors (fig. 4). Quantitative results of factor Xa and thrombin inhibition are given as optical density (OD) on the y-axis in the figures.

Figure 1: Effect of heparin, nadroparin and fondaparinux on DXI pad of DOAC Dipstick in persons without anticoagulant therapy compared with Coamatic chromogenic test

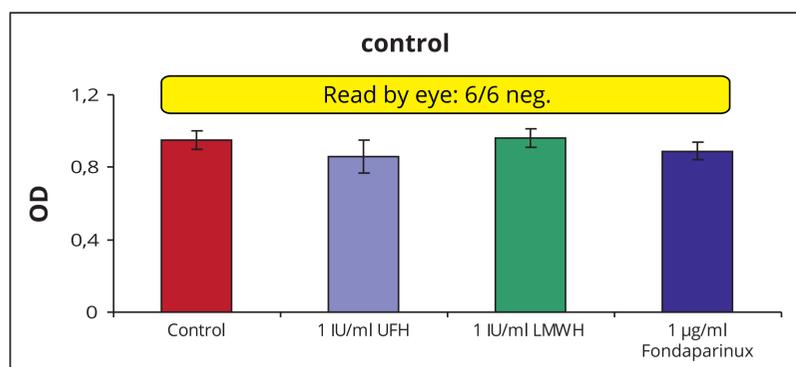


Figure 2: Effect of heparin, nadroparin and fondaparinux on DXI pad of DOAC Dipstick in persons treated with apixaban compared with Coamatic chromogenic test

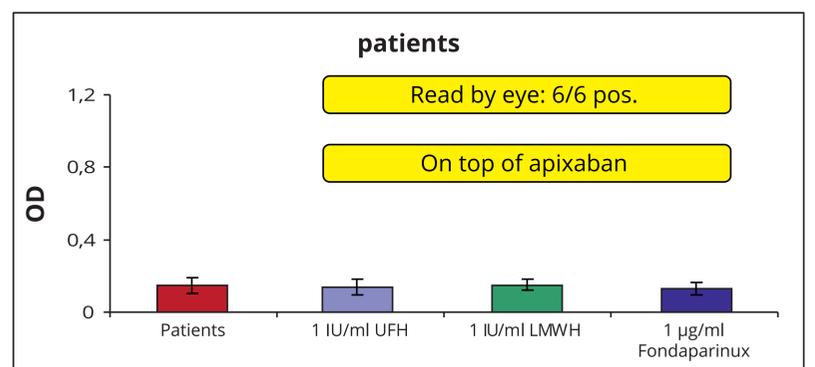


Figure 3: Effect of heparin, r-hirudin and argatroban on DTI pad of DOAC Dipstick in persons without anticoagulant therapy compared with S2238 chromogenic test

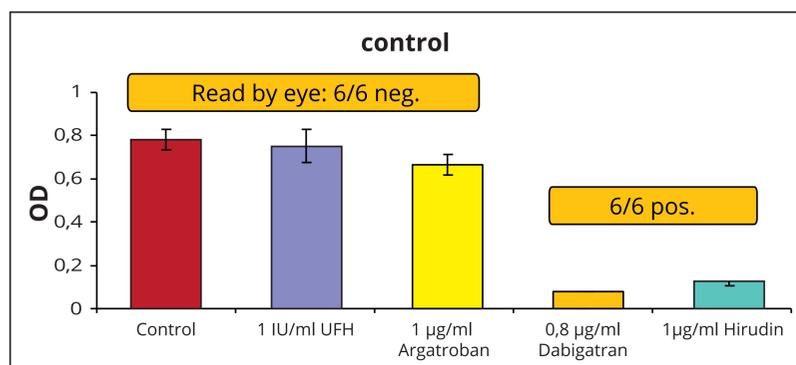
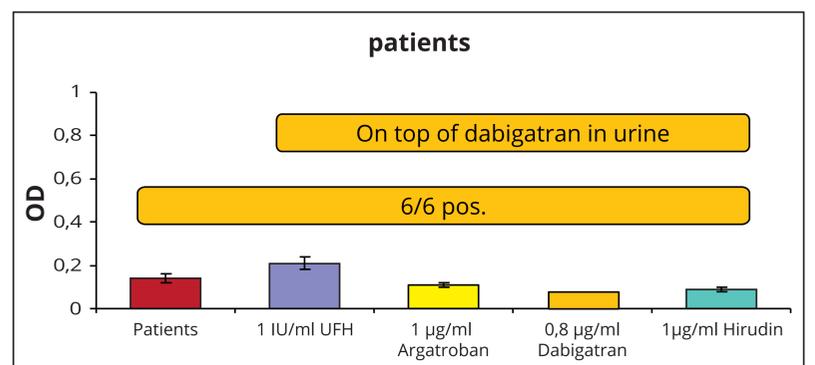


Figure 4: Effect of heparin, r-hirudin and argatroban on DTI pad of DOAC Dipstick in persons treated with dabigatran compared with S2238 chromogenic test



## METHODS

Patient urine samples treated with 110 mg or 150 mg bid DTI (n=6) and 10 mg od rivaroxaban (n=6) and LMWH subcutaneously (n=6) and controls without AC therapy (n=6) were spiked with 0.0, 0.1, 0.3 and 1.0 UFH, LMWH nadroparin (IU/mL), fondaparinux, r-hirudin (µg/mL) and argatroban Z (additional concentration 6 µg/mL). Coamatic and chromogenic S2238 assays were performed to quantify the factor Xa and thrombin inhibition in urine samples, respectively. The study was accepted by the local ethics committee and patients gave written informed consent prior to participation. Colours of factor Xa and thrombin inhibitor pads of DOAC Dipstick after immersion for 2 to 3 sec in urine samples followed by 10 min incubation were adjudicated by trained observers as negative or positive comparing colours to the label of DOAC Dipstick attached to the test tube by visual evaluation according to the instructions for use.