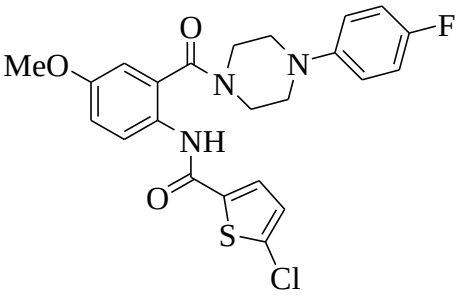
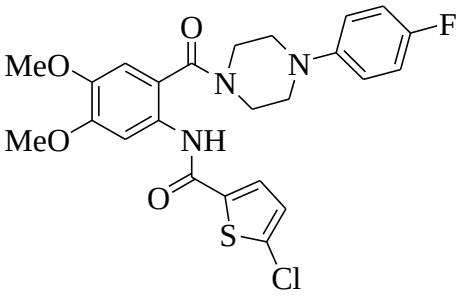
6. CONCLUSION

In an attempt to develop new antithrombotic compounds, a series of anthranilamide derivatives was designed, synthesized and evaluated for their biological activities. From the fifty-nine new analogs some compounds exhibited good to moderate antithrombotic activity. Compound (**201**) and (**208**) exhibited significant FXa enzyme inhibition activity with IC_{50} values 0.61 and 0.74 μM respectively. Evaluation of these compounds for *ex-vivo* anticoagulant activity resulted compounds (**201,** PT= 19.9, aPTT= 40.8 sec.) and (**224,** PT= 13.6, aPTT= 40.0 sec.) exhibiting prolongation in prothrombin and activated partial thromboplastin time than standard drug rivaroxaban (PT= 11.4, aPTT= 37.9 sec.). In haemorrhagic property analysis, they displayed comparable bleeding time at normal antithrombotic dose. Molecular docking and simulation studies as well as physicochemical and ADMET properties calculations further validated their potential for antithrombotic purpose. All these results indicated their favorable selectivity for FXa inhibitory activity and indicated their future potential for antithrombotic development.



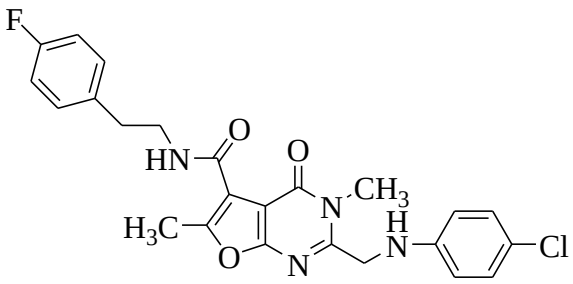
(201)



(208)

A series of furanopyrimidinone analogs designed and synthesized using fragment-based design approach and further evaluated for thrombin inhibitory activity. Compound (**255**) from the series exhibited potent thrombin inhibition activity with IC_{50} value 0.96 μM. In *ex-vivo* anticoagulant evaluation of some potent compounds, (**255**; PT= 18.7, aPTT= 33.4 sec.**)** and (**264;** PT= 11.7, aPTT= 35.3 sec.**)** showed prolongation in prothrombin time compared to control (PT = 8.7 and aPTT = 25.3 sec.). Compound (**255**; BT= 91 sec.) displayed low bleeding time in rats than the standard drug dabigatran (BT= 102 sec.) indicating its safety profile. Other compounds of the series showed submicromolar antithrombotic activity. Molecular docking results provided

favorable binding interactions with thrombin enzyme and ADMET prediction exhibited drug-like potential for these compounds.



(255)