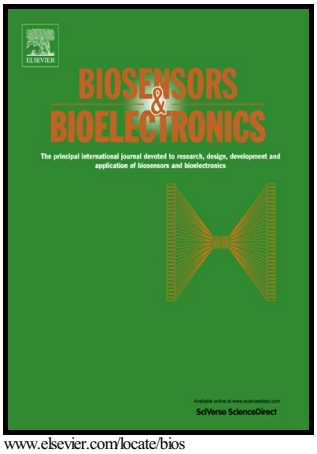

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Nanoplasmonic biosensor device for the monitoring of Acenocoumarol Therapeutic Drug in Plasma

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Abstract

Acenocoumarol (Sintrom®) is an oral anticoagulant prescribed for the treatment of a variety of thromboembolic disorders such as atrial fibrillation and thrombosis or embolism. It inhibits fibrin production preventing clot formation. Acenocoumarol has a narrow therapeutic range, and its effects depend on several factors, such as body weight, age, metabolism, diet, certain medical conditions or the intake of additional drugs, among others. A higher dose may result in the risk of bleeding, while if it is too low, the risk of blood clot can increase. Complementary tools that allow the therapeutic drug monitoring (TDM) of acenocoumarol plasmatic levels from the starting of the treatment would be of paramount importance to personalize the treatment. Point-of-care (POC) devices can offer an added value in facilitating on-site monitoring (i.e. hospitals, primary care doctor or even by the patient itself) and can aid in dosage management. With this aim, we have developed a compact and simple nanoplasmonic sensing device based on gold nanodisks for the rapid monitoring of acenocoumarol, using highly specific polyclonal antibodies produced against this drug. A specific and reproducible label free indirect competitive assay has been developed and the viability of performing the evaluation directly in plasma diluted 1:1 has been demonstrated. A limit of detection (LOD) of only 0.77 ± 0.69 nM, an IC_{50} of 48.2 ± 5.12 nM and a dynamic range between 3.38 ± 1.33 nM and 1154 ± 437 nM were achieved, which easily fit within the drug plasma levels of acenocoumarol, making this approach a highly attractive option for its decentralized monitoring in human plasma.

Keywords: acenocoumarol; LSPR immunosensor; gold nanodisks; point-of-care device

1. Introduction

The nitrophenyl acetyl-4-oxycoumarin or acenocoumarol (commercialized by Novartis as Sintrom®) is a prescribed oral anticoagulant that belongs to the group of vitamin K antagonists. Acenocoumarol is orally administered as a racemic mixture of R (+) and S (-) optical enantiomers that are rapidly absorbed in the gastrointestinal tract and bind to plasma proteins (>99 %) (Vecchione *et al.*, 2007). It decreases the blood's ability to coagulate, inhibits the formation of fibrin protein that together with platelets forms blood clots. It is employed for the prevention and treatment of a wide variety of thromboembolic disorders such as arterial