Immunoassay for rapid detection of oral anticoagulants in blood

CSIC and CIBER-BBN have developed an immunochemical method to detect and quantify coumarin oral anticoagulants, frequently used to prevent deep vein thrombosis, pulmonary embolism, myocardial infarction and stroke. The immunoassay is fast and efficient, and shows detection limits of 5.2 and 15 nM, for acenocumarol and warfarin, respectively, far below the usual plasmatic levels of these drugs

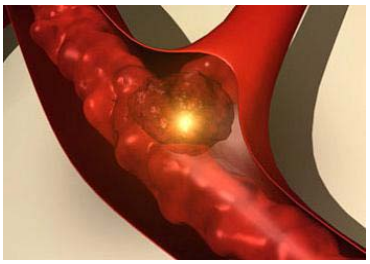
An offer for Patent Licensing and/or R+D collaboration

Sensitive warfarin and acenocoumarol quantification system

It is estimated that about 2% of the population is under treatment with coumarin oral anticoagulants (OAs), such as warfarin (Aldocumar®) or acenocoumarol (Sintrom®). In spite of the appearance of new OAs, in 2011 the U, warfarin expenditures were about $ 144 millions. The main problems associated to these drugs are their narrow therapeutic window and their unpredictable dose-response relationship Thus, there is a large inter and intraindividual variability depending on the genetic isoforms, but also bioavailability is affected by factors such as age, diet, medications, life-style or stress, which raises the need for a personalized adjust of the dose at the beginning of the treatment, but it may also requires to correct it through the treatment time. Moreover, incorrect medication and medication errors are quite frequent due to the great fraction of elderly patients taking such drugs. In 2005, near 25% of the visits to the emergency room at the hospitals, due to adverse drug reactions (ADRs), were due to OAs. Assessment of patient compliance becomes very important in such case, and similarly before emergency surgical interventions of unaware patients.

Current methods for determination of anticoagulants in plasma rely on HPLC or GC-coupled to MS, which are not suitable for rapid and routine monitoring of this drug or performing individual pharmacokinetic studies. We present here an immunochemical method able to quantify plasmatic levels of coumarin anticoagulants. Both, acenocoumarol and warfarin can be detected with limits of detection (LOD) of 5.2 and 15 nM, respectively (IC_{50} of 12.2 and IC_{50} of 6.3 nM, respectively).

The immunoreagents produced do show high avidity for the coumarin OAs and could be used on different immuochemical analytical configurations, including microplate ELISA, test-strip, immunosensors or any other format suitable for further implemtation on Point-of-Care (PoC) devices. In combination with the measurement of prothrombin time, it could provide a complete profile of the drug level for better monitoring of the patient and their response to medication.



Red blood cells forming a clot.

Acenocoumarol and warfarin most frequently used OAs to prevent blood clothing

Main advantages and applications

The main features of the developed technique are:

- Specificity. The cross-reactivity with other compounds different from those of the 4-OH-coumarine family of and their metabolites is negligible.
- High sensitivity. The limits of detection, 5 nM for acenocoumarol and 12 nM for warfarin, are far below the plasmatic concentrations found in patients under OA treatment, which are estimated between 0.03-0.3 μM and 1.5-8 μM, respectively.
- The system is easy to use, fast (less than 30 min), unexpensive and labour-saving. OAs can be directly analysed in plasma, without any previous extraction or pretreatment which is mandatory in the current analytical methods (GC and HPLC).
- In situ application. Special facilities are not required
- It allows routine screening and simultaneous analysis of multiple samples
- Haptens for production of antibodies have been designed to maximise

Patent Status

Spanish patent application filed

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