**Since 1987**
REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS, INTERNATIONAL EDITION | 38 (Sup2):33-34 (2024) Rcpp

**Received**: 26 February 2024 | **Accepted**: 27 February 2024 | **Published**: 5 May 2024

Open Access | Keynote Speech

# Applications of quartz crystal microbalance with dissipation in nanomedicine (QCM-D): a personal experience

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## Abstract
Due to their unique physical and chemical properties, the potential application of nanomaterials in medicine is particularly attractive. Despite the many advantages that nanomaterials can offer as diagnostic and therapeutic tools, their transition from the bench to clinical practice is extremely challenging. One of the many barriers that nanomedicines may encounter is their toxicological effect. In fact, the development of novel nanomaterials / nanoparticles must proceed always in tandem with the assessment of any potential toxicological effects associated to them. Once nanomaterials reach the systemic circulation, they interact with endothelial cells, plasma proteins, and other blood components. There is no doubt that the study of nanomaterials-blood interactions is crucial to warrant the biocompatibility of nanomaterials developed for human use.

**KEYWORDS**
QCM-D, nanomedicine, nanomaterials, nanotoxicology, blood platelets

**How to cite**: Santos-Martinez M. J. Applications of quartz crystal microbalance with dissipation in nanomedicine (QCM-D): a personal experience. *Rev. Clin. Pharmacol. Pharmacokinet. Int. Ed.* 38 (Sup2): 33-34 (2024).
https://doi.org/10.61873/FKIQ6626

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## MAIN MESSAGE

Most of the current research in nanomedicine is devoted to the design of nanomaterials for diagnostic and therapeutic applications. However, nanomedicines, independently of their route of administration, will eventually reach the blood stream and interact with plasma proteins and, among other cells, with erythrocytes, platelets, and white blood cells [1]. Investigating the interactions of nanomaterials with biological systems, and particularly with blood components, is crucial for the development and optimisation of nanomaterials, as blood incompatibilities such as haemolysis, bleeding or thrombosis, among others, could result in serious side effects that may prevent their successful clinical translation. Therefore, the careful assessment and characterisation of nanomaterial interactions with blood is of critical importance as part of the development process of nanomedicines.

The principle of analysis of a quartz crystal microbalance (QCM) is based on changes of the resonance frequency of a quartz crystal when an alternating electric field is applied across the crystal. Material adsorption on the surface of the crystal results in a decrease in the frequency of vibration that is proportional to the mass that can be quantified using the Sauerbrey equation [2]. In fact, when the adsorbed layer is thin and rigid, the mass can be accurately calculated using this equation. However, the measurement of changes of the frequency alone does not offer any information about the viscoelastic characteristics of the deposited layer and, when the layer is soft and thick, the mass can be underestimated when the Sauerbrey equation is applied. The QCM with dissipation technology (QCM-D) however, measures, in addition to changes in frequency, the called "dissipation factor". This parameter is related to the viscoelastic properties of the adsorbed layer, and it can be used (i) to monitor its conformational and structural changes at real time and, together with the frequency, (ii) to calculate the mass and thickness of thick and viscoelastic layers using specific mathematical models [3]. We have applied this technology for looking at the interactions between nanoparticles developed for drug delivery and their targets [4], and the potential barriers that they must overcome to exert their action [5]. Our research team has developed a novel method for the quantification and characterization of platelet aggregation under flow conditions using a QCM-D that closely mimics the conditions encountered in the microvasculature [6]. We have demonstrated that this methodology, due to the sensitivity of the device, allows the detection of platelet microaggregates; the very initial process of thrombus formation. During the past years we have applied our approach for investigating the effect of different compounds, nanomaterials, and novel formulations on platelet function [7-10]. Our work supports the idea that ours is a unique approach for looking at platelet-nanomaterials interactions and for investigating the blood compatibility of nanomaterials.

## ACKNOWLEDGEMENTS

The author acknowledges the collaborators and researchers that have made possible this research over the years, and our generous blood donors.

## CONFLICT OF INTEREST STATEMENT

The author declares no conflicts of interest.

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