

Vibrational Spectroscopic Investigation of Drug-Target-Interactions in Malaria Research

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Raman and IR spectroscopy was applied an investigation of the molecular mode of action of antimalarial active agents with their biological targets [1-8].

While Malaria is still one of the most devastating infectious diseases on earth [9, 10], resistances against established drugs arise on a global scale [11-13]. However, the molecular mode of action of those key drugs, e.g. chloroquine, is not well understood. It is believed that this class of antimalarials acts in the red blood cell state of the plasmodium's asexual life cycle in the human body. At this stage the drugs interfere with the detoxification process of the hemoglobin digestion by-products [14, 15].

In this contribution we demonstrate the high potential of Raman spectroscopy for a non-invasive, label-free, molecular investigation of important antimalarial active agents [1-5] and the malaria pigment hemozoin [6] as well as their molecular interactions [7, 8]. UV resonance Raman microscopy was applied for a very sensitive and selective investigation of different drugs under physiological conditions [1-4]. The experimental results have been confirmed by means of DFT calculations. Also the biological target hemozoin was localized in the infected cells and structurally investigated [6]. These *in situ* results were compared with spectra of extracted hemozoin as well as with synthesized β -hematin [6] and the Raman spectra of dimeric unit cell of the malaria pigment were calculated for the first time. A new, versatile device for Raman difference spectroscopy was designed and allows for a gentle, sensitive, selective, and precise investigation of drug target interactions [8].

The understanding of molecular vibrations of the active agents and the targets and how they may change upon molecular interactions with each other will inform drug chemistry and help fighting back against Malaria.

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