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Photo-reactivity assessment of perfusion drugs combining quantum chemical approach and experimental studies

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The susceptibility of a drug substance or drug product to degrade upon light exposure is far from being an uncommon property. Actually, the number of drugs found to be photo-chemically unstable is steadily increasing and the European Pharmacopoeia recommends light protection for hundreds of medical drugs and a number of adjuvants. The evaluation of interactions between drugs and light accounts for a natural part of the research and development work for new medical products. This allows the formulations containing drugs susceptible to photoreactions to be marked and adequately stored. However, in some situations, the ideals are not always maintained. Indeed, it is well known that in-use conditions do not always coincide with the control or design spaces, within which,it has been shown that the drug is stable. In this context, liquid preparations are much more concerned than solid formulations of the corresponding drug substances, being usually far more photolabile. That's why elucidating photo degradation mechanisms of drug products can be of paramount importance in that this can help reckon whether special procedures or additives could be usedto prevent any loss of drug potency and formation of photo products during their handling and administration. We present here an approach combining a computational method based upon the density functional theory (DFT) and experimental studies using liquid chromatography-multistage mass spectrometry (LC-MS^n) to investigate the photo degradation behaviour of parenteral drugs through two case studies, tirofiban and raltitrexed. The results predicted by DFT were experimentally supported through the photo products identification. As their photoreactions were shown to mainly proceed through type I and type II photosensitization mechanisms, the possibility of adding quenchers to the formulation can be considered. The major contenders would be substances such as ascorbic acid, a-tocopherol, and BHT, which are capable of acting as free radical scavengers and weak singlet oxygen quenchers.

Biography

Bernard Do has completed his PhD at the age of 29 years from Paris-Descartes University (France). He is hospital pharmacist, associate professor and senior researcher of a research team focusing on drug intrinsic stability and drug/polymer interactions, at Assistance Publique-Hôpitaux de Paris and Paris-Saclay University. He has published more than 40 papers in reputed journals and serving as an editorial board member of repute.

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