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The characterisation of methadone hydrochloride crystals using Confocal (CM) and Scanning Electron Microscopy (SEM)

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Statement of the Problem: Information about the crystalline structure of methadone hydrochloride (MDN) is historical and based on the use of light microscopy, which is limited because it cannot analyse 3D objects or provide comprehensive information about crystal dimensions.

Purpose: The purpose of this study is to develop new microscopic techniques, using the CM and SEM, to characterise MDN crystals and to standardise their detection and measurement.

Methodology & Theoretical Orientation: MDN was crystallised using two different solvents, warm rhodamine solution (0.0001% g/mL) and warm HPLC grade water. Seven slides were prepared using MDN-rhodamine and MDN-water solutions for CM and SEM work respectively. For each test, six crystals were observed from each slide (n=42 crystals). For dimensional measurements, top and vertical views were observed using SEM, while a Z-stack technique was used in CM.

Findings: CM and SEM images showed diamond shaped MDN crystals. Independent samples t-test between SEM and CM readings of crystals dimensions showed significant differences regarding crystals length ($t(82)=5.14$, $p<0.05$) and width ($t(82)=4.72$, $p< 0.05$). SEM measurements revealed a longer crystal (mean 46.4±15.2 μm) than CM measurement (32±8.3 μm). SEM width measurements were significantly greater (mean 28.03±8.2 μm) than CM readings (20.85±5.5 μm). Mann-Whitney U Test showed significant differences in MDN crystals thickness when measured by SEM and confocal microscopy ($U=1283$, $p<0.05$); SEM exhibited significantly thinner crystals (6.62±2.9 μm) than CM measurements (9.6±4.6 μm).

Conclusion & Significance: The CM technique could not be recommended to measure MDN crystals dimensions because of the staining dye artefacts. SEM measurements were considered more accurate as they reflect the actual thickness of MDN crystals. The SEM technique shows a potential for the identification of MDN in forensic science.

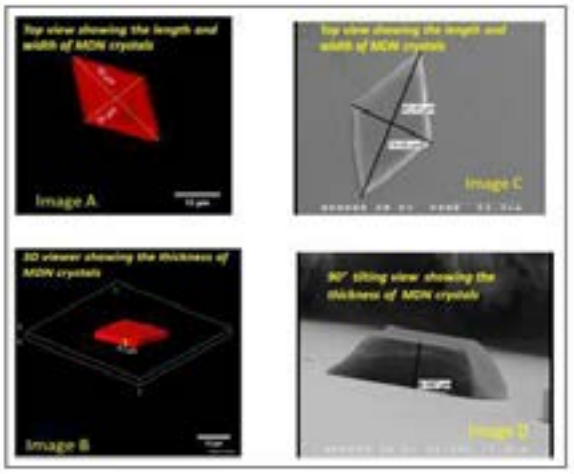

Figure 1: Photomicrographs of MDN crystals using CM and SEM techniques.

Recent Publications

1. Ren F, Su J, Xiong H, Tian Y, Ren G and Jing Q (2017) Characterization of ibuprofen microparticle and improvement of the dissolution. Pharmaceutical Development and Technology. 22(1):63-68.
2. Singh M R, Chakraborty J, Nere N, Tung H H, Bordawekar S and Ramkrishna D (2012) Image analysis based method for 3D crystal morphology measurement and polymorph identify cation using confocal microscopy. Crystal Growth & Design. 12(7):3735-48.
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4. Addo R T, Yeboah K G, Siwale R C, Siddig A, Jones A, Ubale R V, et al. (2015) Formulation and characterization of atropine sulfate in albumin– chitosan microparticles for *in vivo* ocular drug delivery. Journal of Pharmaceutical Sciences. 104(5):1677-90.
5. Hubach C, Jones F (1950) Methadone hydrochloride optical properties, microchemical reactions, and x-ray diffraction data. Analytical Chemistry. 22(4):595-8.

Biography

Noor Al Hasani has finished her Bachelor's degree in Pharmacy at Bagdad College of Pharmacy in 2006, Iraq. After three years of working as a Pharmacist at different hospitals in Iraq, she started studies for her Master's degree in Clinical Pharmacy from Baghdad University, College of Pharmacy in 2011. She was assigned in November 2011 as Assistant Lecturer at University of Bagdad, College of Dentistry, teaching Pharmacology for undergraduate students. In October 2014, she joined a PhD programme at King's College London working with Prof. Kim Wolff and Dr. Paul G Royall to design a new abuse- deterring formulation of methadone hydrochloride.

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