Probing the effect of non-/hydrostatic pressures on ofloxacin and levofloxacin

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BACKGROUND

How can we improve the current, often iterative tablet formulation process?
With a deeper understanding of pharmacologically relevant materials:
- Structural characteristics
- Behaviour under pressure
Within the pressure range used in the tablet manufacturing process (i.e., < 1000 MPa)

DIAMOND ANVIL CELL (DAC)

- Used to carry out pressure studies to follow changes in the internal structures of crystalline materials
- Diamond culets allow electromagnetic radiation to pass through (e.g. X-rays)
- Pressure is monitored using ruby fluorescence
- A hydrostatic environment can be achieved with a pressure transmitting medium (PTM):

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Abbrev.</th>
<th>Hydrostatic limit (GPa)</th>
<th>Solubility</th>
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<tbody>
<tr>
<td>Petroleum ether</td>
<td>Pet</td>
<td>~ 6 [2]</td>
<td>Inert</td>
</tr>
</tbody>
</table>

OFLOXACIN AND LEVOFLOXACIN

(OA) Potential phase transitions observed
- Collect single crystal X-ray diffraction data for structural comparison
- Mimic non-hydrostatic environment using a PTM with a low hydrostatic limit (e.g. Silicone oil)
- Different rate of compression under hydrostatic and non-hydrostatic pressure, potentially linked to an increase in particle fragmentation due to more particle-particle interactions being present
- Collect PXRD data for OH and LH to compare against OA

X-RAY POWDER DIFFRACTION (XRPD)

- OA Pet displays similar behaviour to OA 4:1 M-E, but slightly broader peaks
- Solubility of OA in 4:1 M-E helps maintain crystallinity upon compression
- Potential reversible phase transition (PT) at 7000 MPa for OA in 4:1 M-E

CONCLUSIONS & FUTURE WORK

- Overall smooth and steady reduction in unit cell parameters
- OA in no PTM appears to be systematically less compressible than in a hydrostatic PTM
- Increase in particle fragmentation?
- Potential PT for OA in no PTM at 2000 MPa

REFERENCES

[4] Bryant et al., CrystEngComm, 2018, 20, 2698

(Above) Table summarising the crystal structures studied, their predicted slip planes and whether they display hydrogen bonding interactions bridging across the slip plane slabs:
(Below) (a) Chemical structure of ofloxacin and levofloxacin (b-d) Structures and topological surfaces for the predicted slip planes of (b) LH (c) OA (d) LAZ (e)