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FUTURE MANUFACTURING RESEARCH HUB

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

SCAN ME

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BACKGROUND

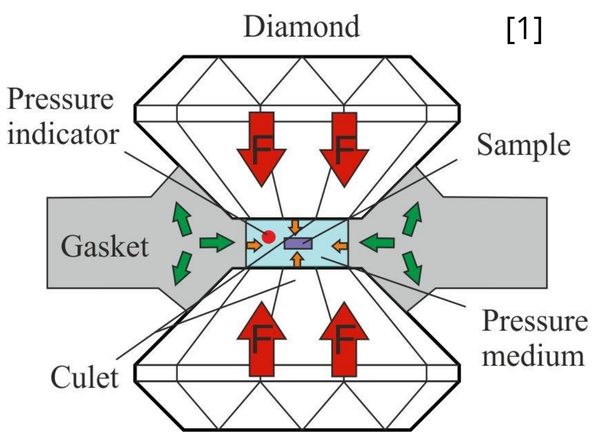
How can we improve the current, often iterative tablet formulation process?

With a deeper understanding of pharmaceutically 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



[1]

How does it work?

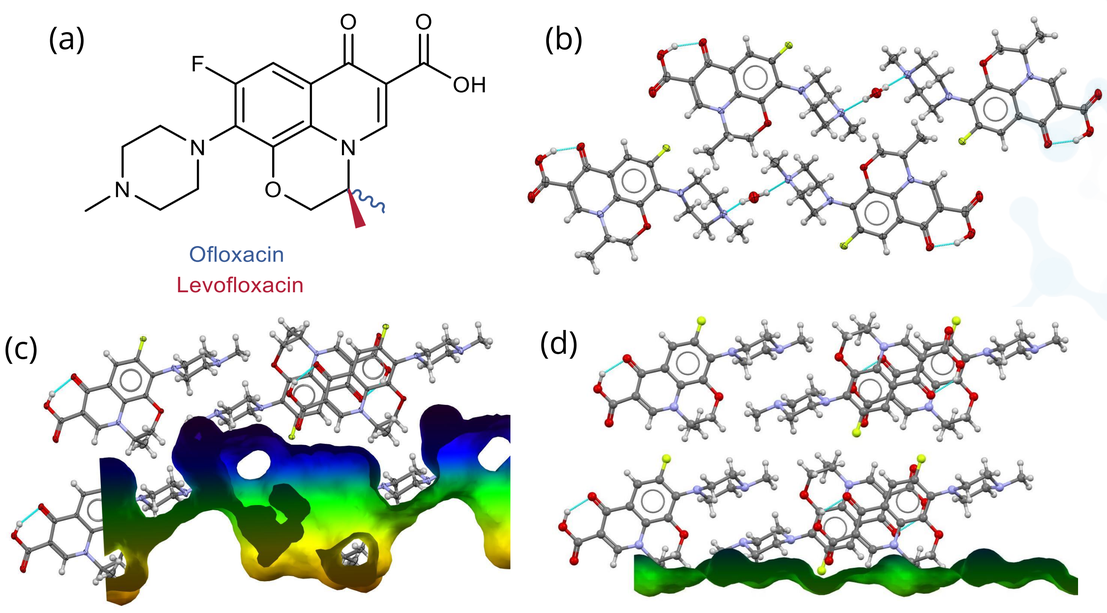
- Diamond culets allow electromagnetic radiation to pass through (e.g. X-rays)
- Pressure is monitored using ruby fluorescence
- A hydrostatic environment can be achieved with a pressure transmitting medium (PTM):

Solvent	Abbrev.	Hydrostatic limit (GPa)	Solubility
Petroleum ether	Pet	~ 6 [2]	Inert
4:1 Methanol:ethanol	4:1 M-E	~ 10.5 [3]	Slight solubility in OA and LHY

OFLOXACIN AND LEVOFLOXACIN

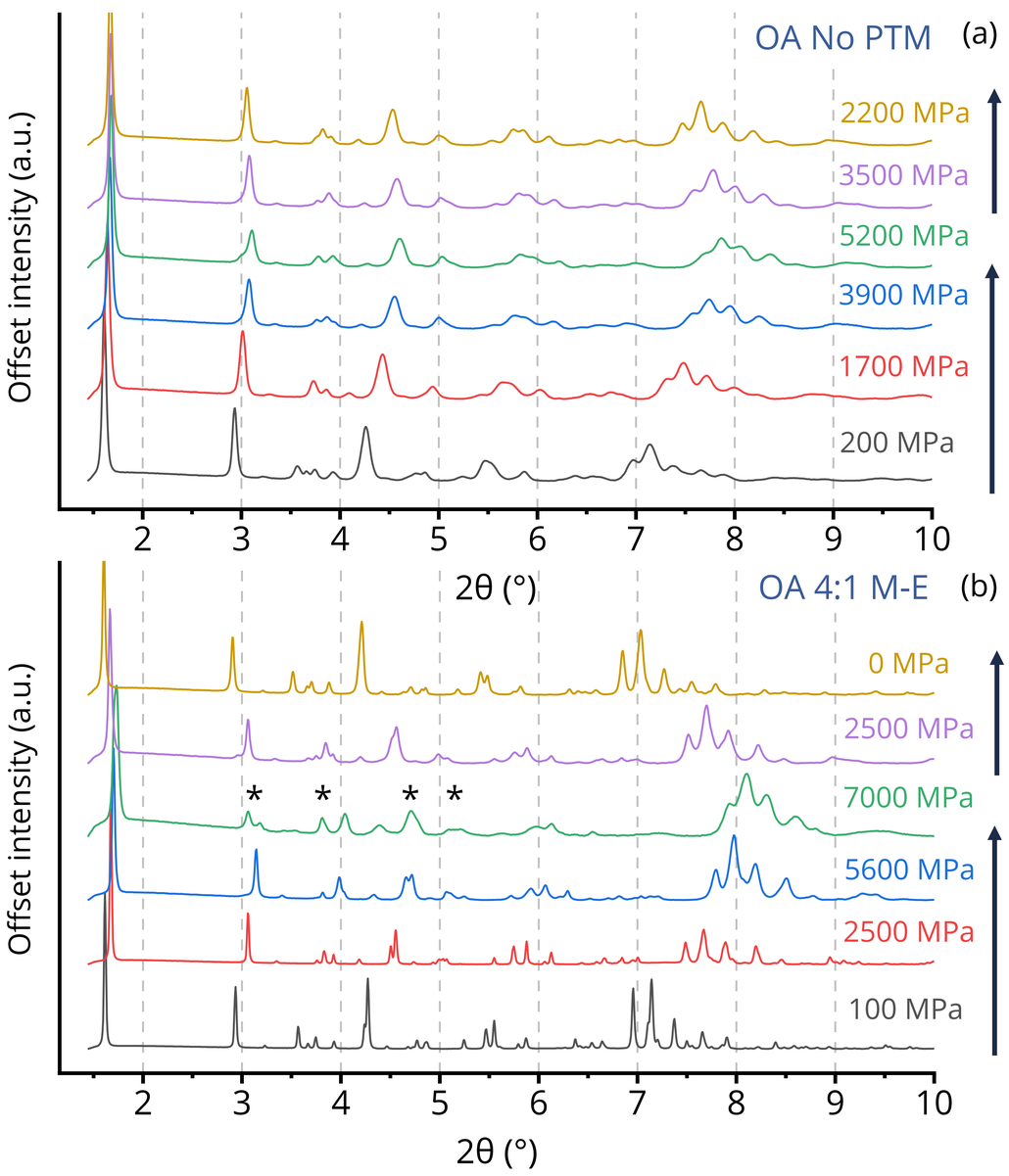
Sample	Abbrev.	CSD refcode	Space group	Slip plane(s)	Hydrogen bonded
Levofloxacin hemihydrate	LH	YUJNUM01	C2	-	N/A
Levofloxacin anhydrate Y form	LAY	LICWOM	C2	(200)	No
Ofloxacin anhydrate	OA	CUYCEF	C2/c	(20-2)	No

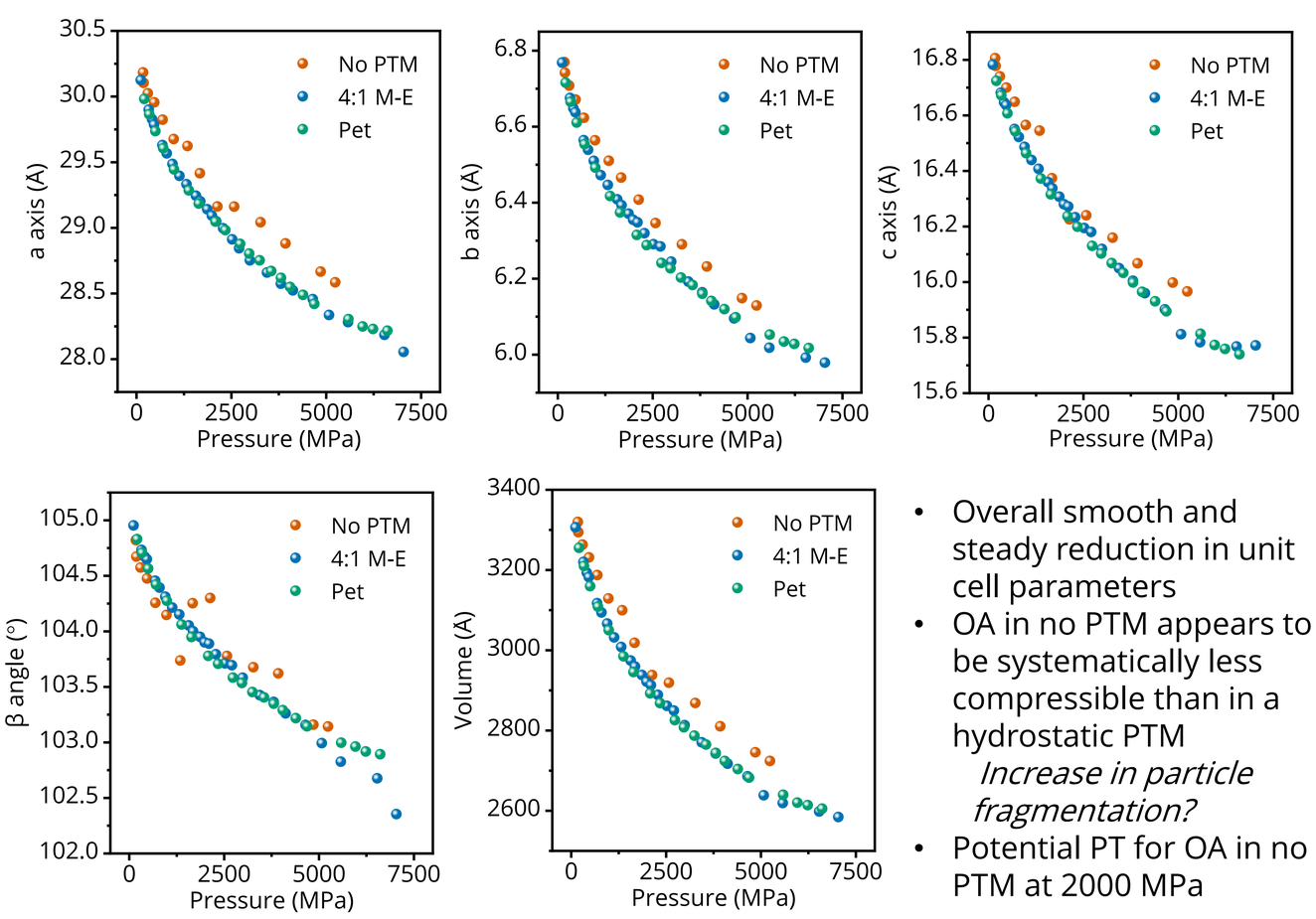
(Above) Table summarising the crystal structures studied, their predicted slip planes and whether they display hydrogen bonding interactions bridging across the slip plane slabs; (Below) (a) Chemical structure of ofloxacin and levofloxacin (b-d) Structures and topological surfaces for the predicted slip planes of (b) LH (c) OA (d) LAY [4]



- Powder X-ray diffraction data under hydrostatic (Pet, 4:1 M-E) and non-hydrostatic (no PTM) pressure was collected at ESRF (beamline ID15B)

X-RAY POWDER DIFFRACTION (XRPD)





Plots of XRPD during non-hydrostatic (a) and hydrostatic (b) compression & decompression

- 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
- 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

CONCLUSIONS & FUTURE WORK

- ☑ 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 LAY and LH to compare against OA

REFERENCES

[1] N. Waeselmann, *PhD thesis*, University of Hamburg, 2012; **[2]** N. Tateiwa *et al.*, *Rev. Sci. Instrum.*, 2009, **80**, 123901; **[3]** S. Klotz *et al.*, *J. Phys. D: Appl. Phys.*, 2009, **42**, 075413; **[4]** Bryant *et al.*, *CrystEngComm*, 2018, **20**, 2698