



# Glutathione-Sensitive Nanocarrier Covalent Organic Frameworks for the Synergistic Release of Chemotherapeutics

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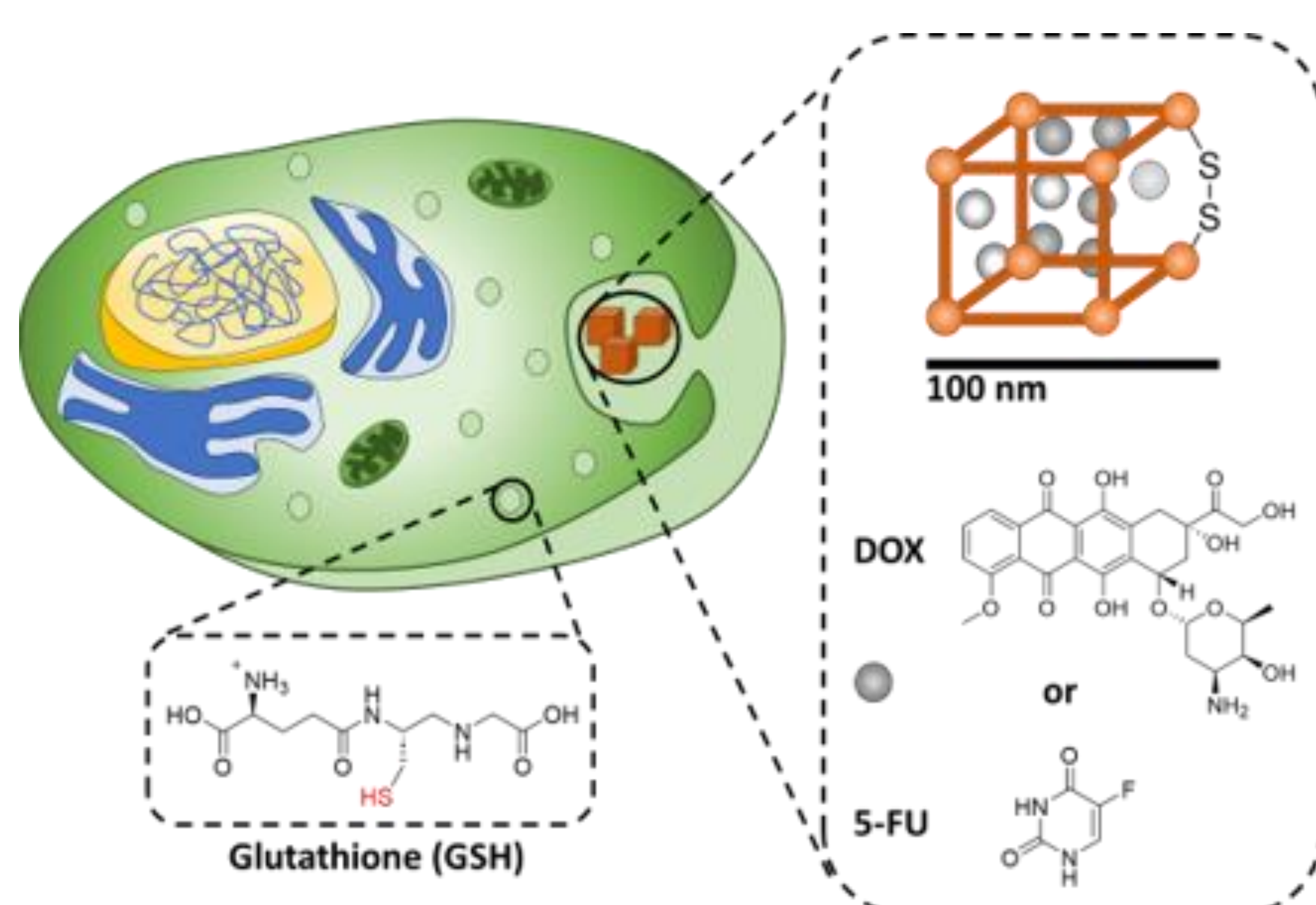
## Molecular Organic Framework (MOF)

Molecular Organic Frameworks, known as MOFs are porous, crystalline structures that are made up of metal centers bonded to organic linkers. Depending on the metal ion and linker, the size of the pores and geometry of the molecule can vary greatly. These pores can absorb and encapsulate other molecules, depending on both the size of the molecule and the pores, as well as potential intermolecular interactions between the molecule and framework. By changing the linkers, you can also alter the functionality of the MOF. This gives MOFs a wide variety of applications, such as filtration and drug delivery.

## Our MOF Project

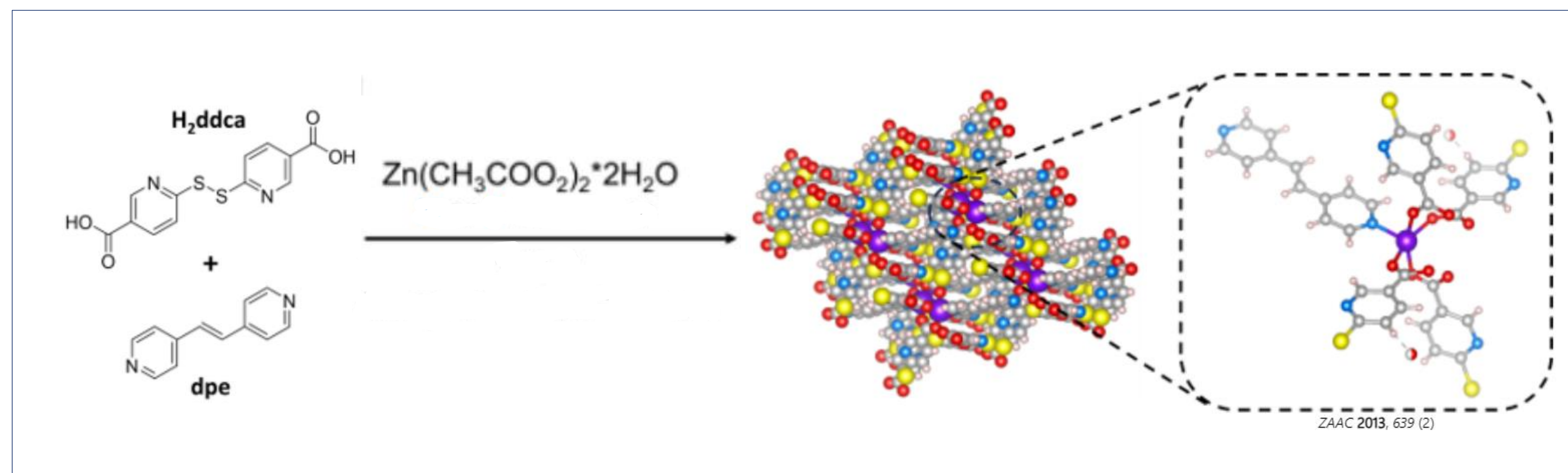
This project uses a Zn-based MOF as a nanocarrier for chemotherapeutics, specifically doxorubicin and 5-fluorouracil. Using this MOF is important because of its ability to selectively transport the cancer drug to malignant cells, which will limit side effects that are often associated with these medications. The reason this is possible is because of the dithiol present in our organic linker. Glutathione is a peptide found in the body in all cells, but much more prominently in cancer cells, with a concentration up to 1000x higher than in healthy cells. This peptide breaks down S-S bonds in the body, so it will also break down our MOF, releasing the drug into the cell. The hope is that because of the higher concentration of glutathione in cancer cells, the MOF will go to these cells and break down and release the medication in primarily the sick cells and not the healthy cells. This will lower overall side effects because the healthy cells would be less effected by the medication.

## Redox-Responsive Nanoparticles

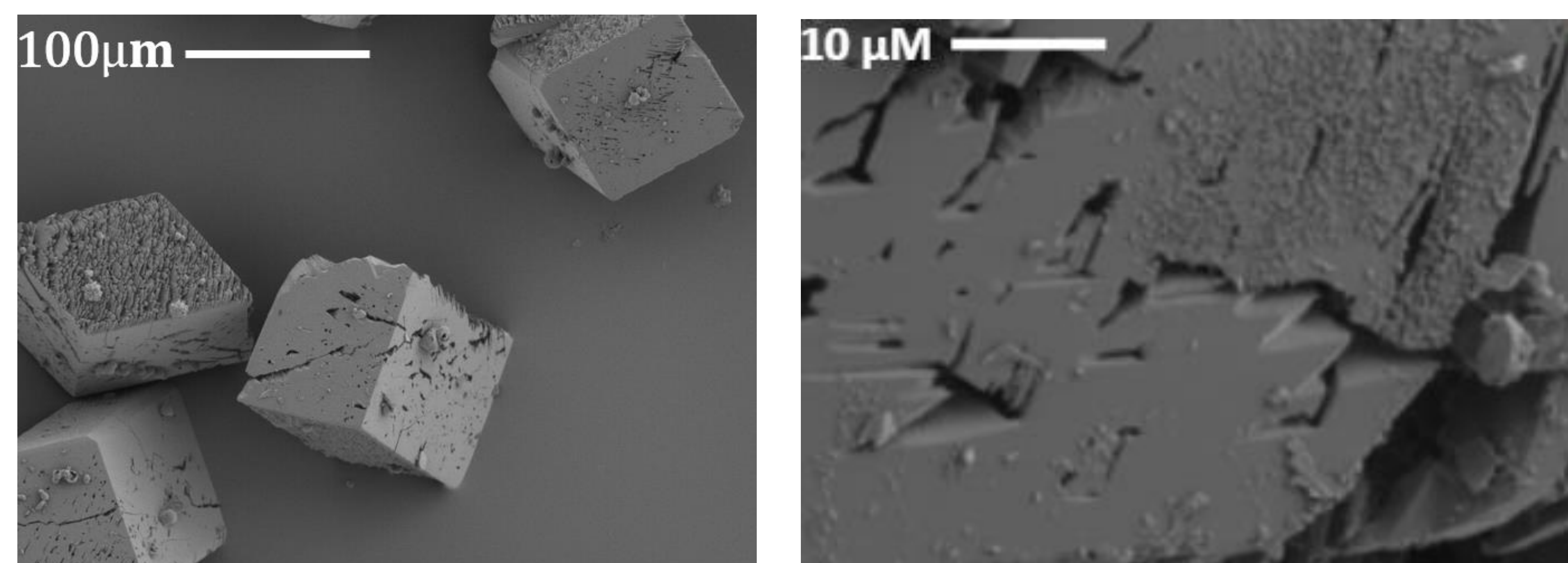


How MOF containing chemotherapeutics Doxorubicin and 5-fluorouracil is broken down inside of cells using glutathione, which is up to 1000x more present in cancer cells

## Synthesis of Zinc-based MOF: $[Zn_2(ddca)_2(dpe)]_n \cdot nH_2O$



## Characterization



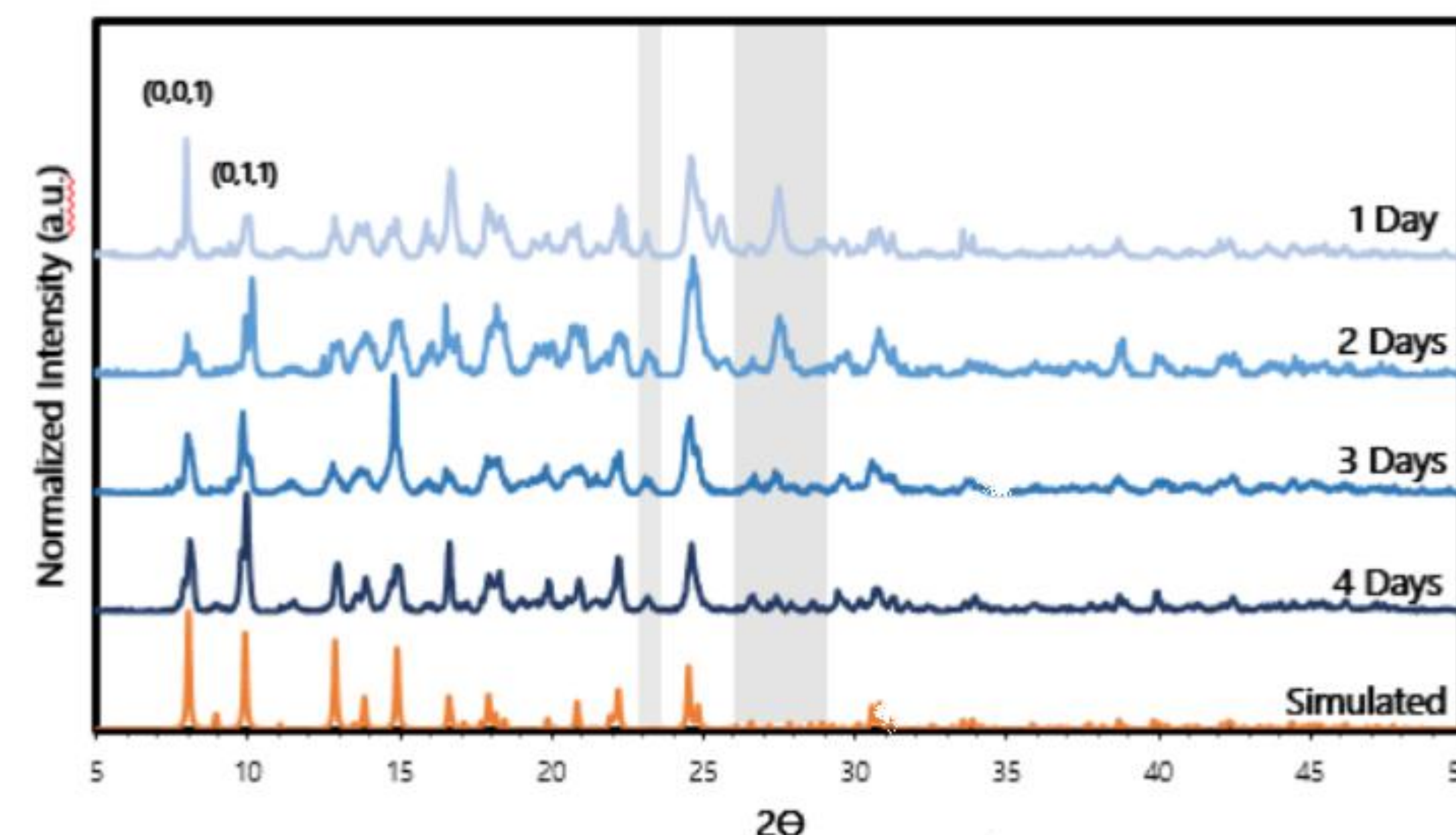
Scanning electron microscope (SEM) images of  $[Zn_2(ddca)_2(dpe)]_n \cdot nH_2O$

## Powder X-Ray Diffraction (PXRD)

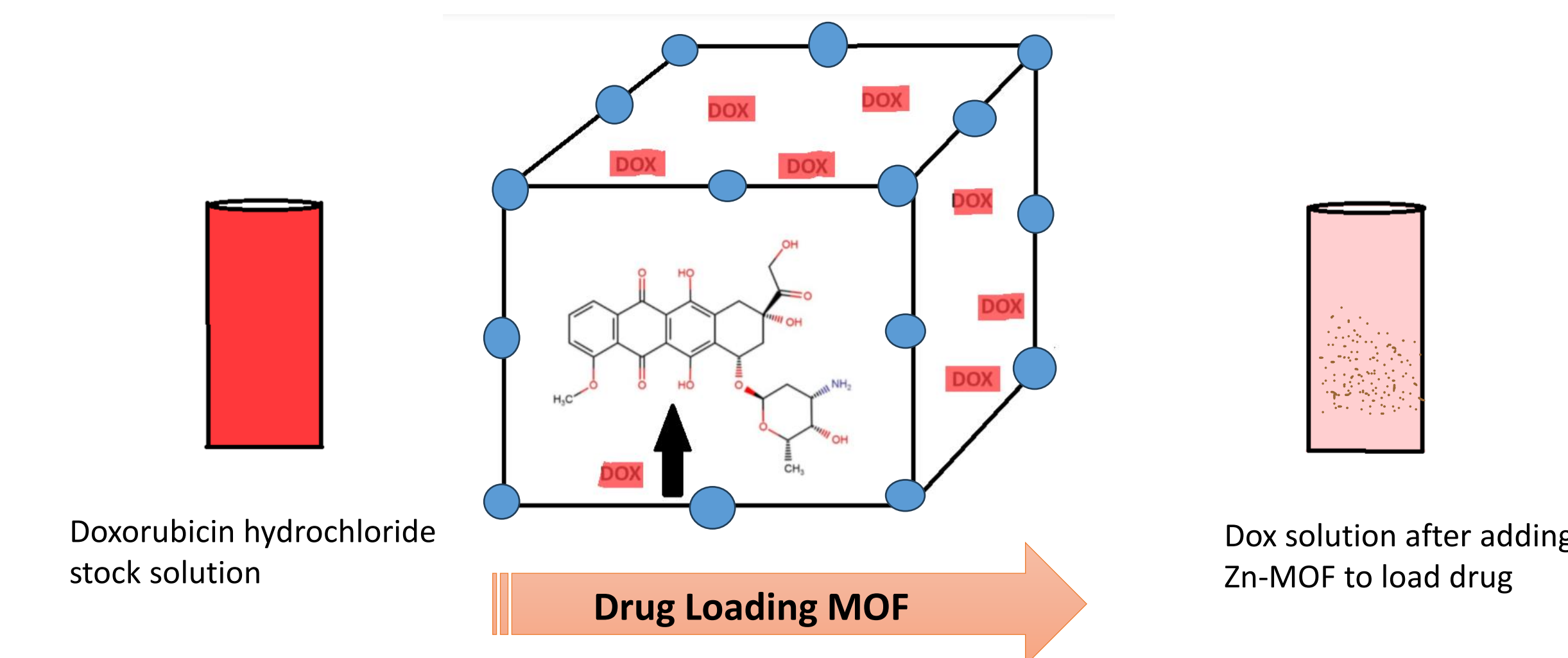
### What is PXRD?

PXRD is a characterization technique that measures diffraction patterns in materials using X-Ray waves. Smaller  $2\theta$  values correlate with larger interatomic distance, which is evidence of present pores and crystallinity in the material. MOFs are known to show strong peaks at low  $2\theta$  values

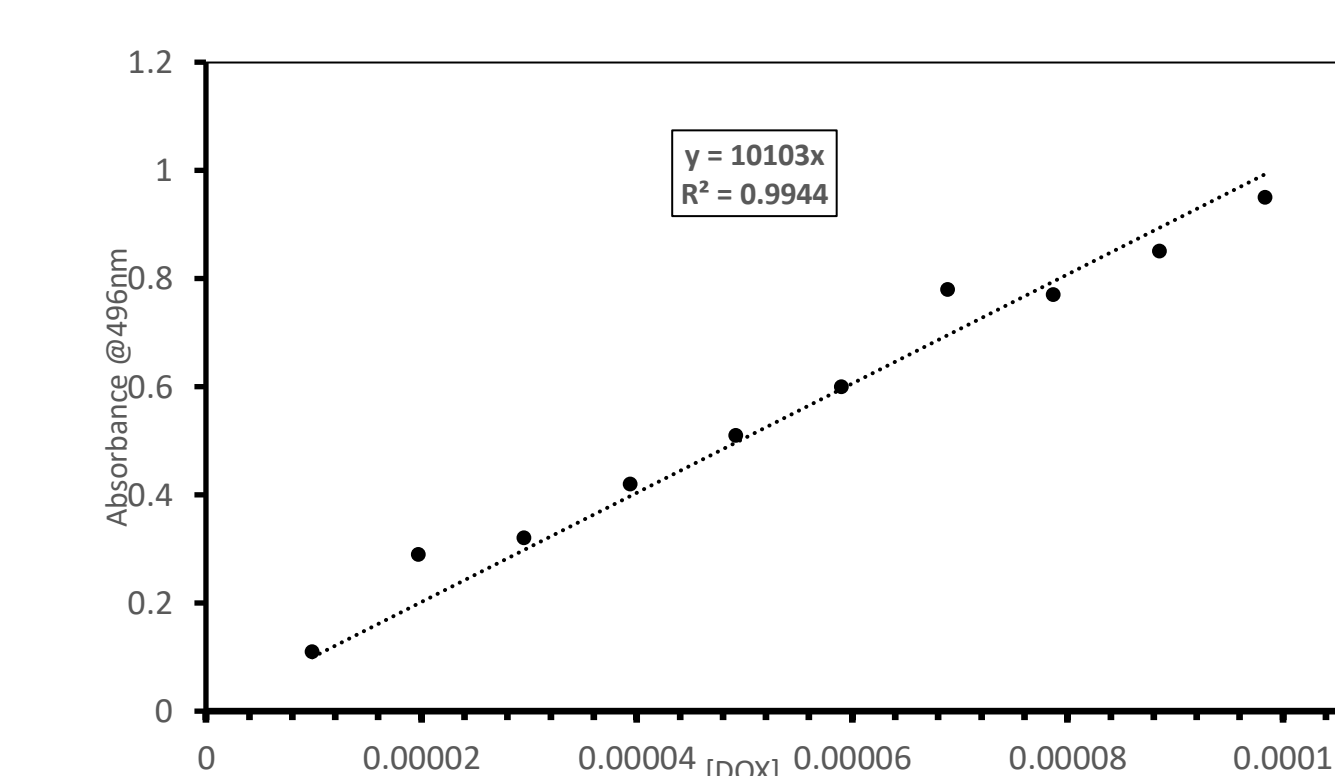
PXRD of  $[Zn_2(ddca)_2(dpe)]_n \cdot nH_2O$  showing longer synthetic timing correlating to loss of starting material into product



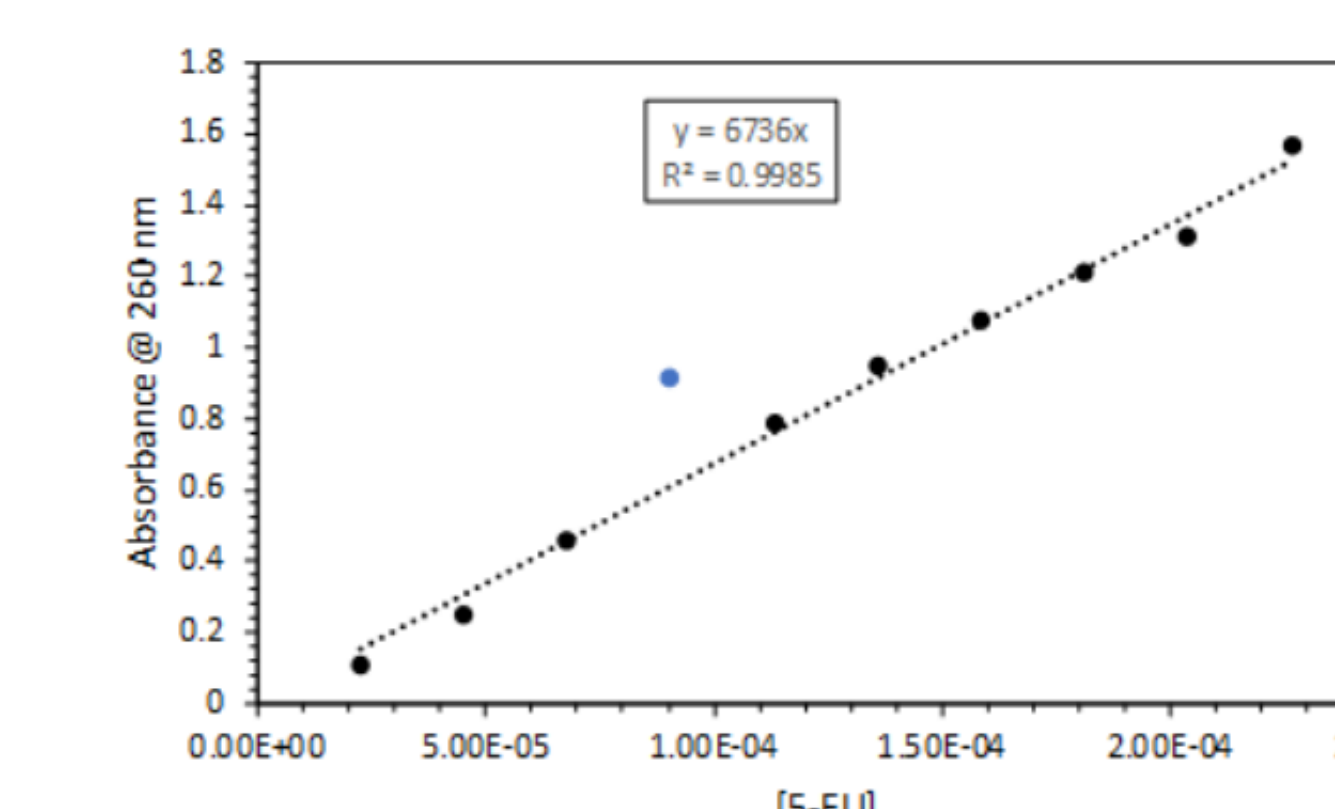
## Chemotherapeutic Loading



Drug Loading of Doxorubicin into  $[Zn_2(ddca)_2(dpe)]_n \cdot nH_2O$ ; the DOX solution lightens up as the drug is loaded into MOF because of a decrease in concentration of doxorubicin in the solution



Sample	Abs @496nm	[DOX] stock	[DOX] after loading	$\Delta$ [DOX]
1	0.91	1.05E-4 M	9.398E-5 M	1.089E-5
2	0.96	1.05E-4 M	9.91E-5 M	5.77E-6
3	0.93	1.05E-4 M	9.61E-5 M	8.77E-6



Sample	Abs @260nm	[5-FU] stock	[5-FU] after loading	$\Delta$ [5-FU]
1	1.721	3.5E-4 M	2.55E-4 M	9.5E-5 M

Calibration curve of doxorubicin hydrochloride and 5-fluorouracil stock solution concentration and comparing before and after concentration of stock solution with the addition of  $[Zn_2(ddca)_2(dpe)]_n \cdot nH_2O$  to load pores with chemotherapeutic

## Acknowledgements

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## References

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- (2) Kirlikovali, K. O.; Hanna, S. L.; Son, F. A.; Farha, O. K. Back to the Basics: Developing Advanced Metal–Organic Frameworks Using Fundamental Chemistry Concepts. *ACS Nanosci. Au* **2023**, 3 (1), 37–45. <https://doi.org/10.1021/acsnanoscienu.2c00046>.