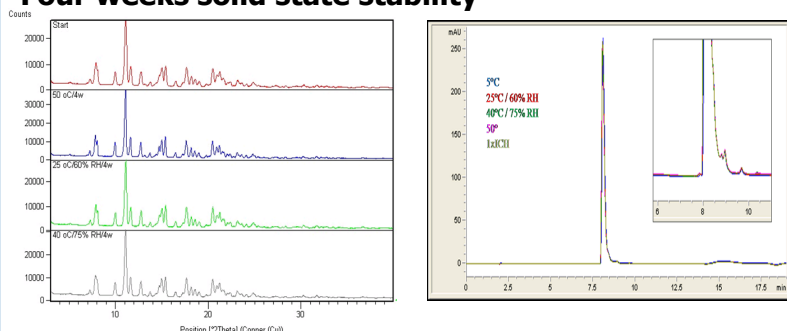


# Solid State Chemistry Case Study: Solid and Solution Stability and Solubility of a Crystalline Form of a Novel 15-membered Azalide Derivative

## Objective:

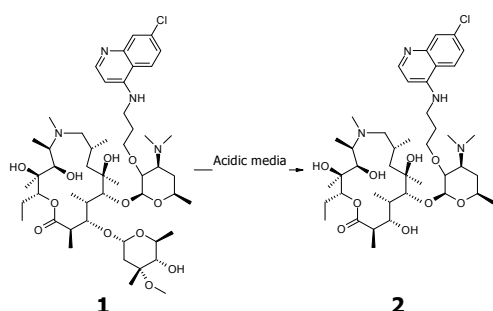
- To determine the solid state stability (4 weeks), light stability and stability and solubility in buffers and biorelevant media of a crystalline form of 2'-O-{3-[(7-chloro-4-quinolinyl)amino]propyl}-9--deoxy-9a-methyl-9a-aza-9a-homoerythromycin A, a novel 15-membered azalide

## Four weeks solid state stability



Condition	DSC		TGA
	$\Delta H$ (J/g)	Onset (°C)	$-\Delta$ Mass (mg)
Start	66.6	206.6	0.4
50 °C, closed, dark	69.3	206.3	0.3
25 °C/60% RH, closed, dark	68.8	206.5	0.4
40 °C/75% RH, closed, dark	66.2	206.0	0.4

## Four weeks solution stability



Medium	% of compound 1 after 4 weeks		
	5 °C	25 °C	50 °C
pH 2 (Phosphate buffer)	44.4	0.0	0.0
pH 3 (Citrate buffer)	89.9	35.0	0.0
pH 4 (Citrate buffer)	99.5	91.8	12.9
pH 5 (Citrate buffer)	99.6	99.1	81.5
pH 6 (Citrate buffer)	100.0	97.4	80.9
pH 7 (Phosphate buffer)	99.3	87.9	43.3
pH 8 (TRIS)	98.9	80.9	40.4

## Solubility

Medium	Solubility (mg/ml)		Medium	Solubility (mg/ml)	
	Initial	24 hours		Initial	24 hours
pH 2 (Phosphate buffer)	10.5	Degrade	pH 8 (TRIS)	0.05	0.06
pH 3 (Citrate buffer)	10.5	Degrade	Water	0.03	0.04
pH 4 (Citrate buffer)	10.4	10.6	SGF (pH 1.6)		>10
pH 5 (Citrate buffer)	7.2	7.8	FastedSIF (pH 5.0)		>7
pH 6 (Citrate buffer)	3.4	3.6	FedSIF (pH 6.5)		>3
pH 7 (Phosphate buffer)	0.4	0.5			

## Summary:

Solid state stability studies for up to 4 weeks showed that a crystalline form of 1 is physically and chemically stable. Stability of 1 in solutions is pH and temperature dependent, and is most stable at pH 5 to 6 and at 5 °C and 25 °C. Solubility of 1 is pH dependent and is high at pH values < 6. Degradation of 1 in aqueous acidic media is due to hydrolysis of the cladinose sugar

**References :** D. Filić et al., J. Pharm. Sci. 2011, 2586–2598