

Crystallization and Characterization of Cocrystals of Piroxicam and 2,5-Dihydroxybenzoic Acid

E. M. Horstman,^a J.A. Bertke,^b E. H. Kim,^a L. C. Gonzalez,^a G. G. Z. Zhang,^c Y. Gong,^{c*} and P. J. A. Kenis^a

^a Department of Chemical & Biomolecular Engineering, University of Illinois at Urbana-Champaign, 600 South Mathews Avenue, Urbana, Illinois 61801, USA.

^b School of Chemical Sciences, University of Illinois at Urbana-Champaign, 505 South Mathews Avenue, Urbana, Illinois 61801, USA.

^c Drug Product Development, Research and Development, AbbVie Inc., 1 North Waukegan Road, North Chicago, Illinois 60064, USA.

Chip Fabrication and Assembly.

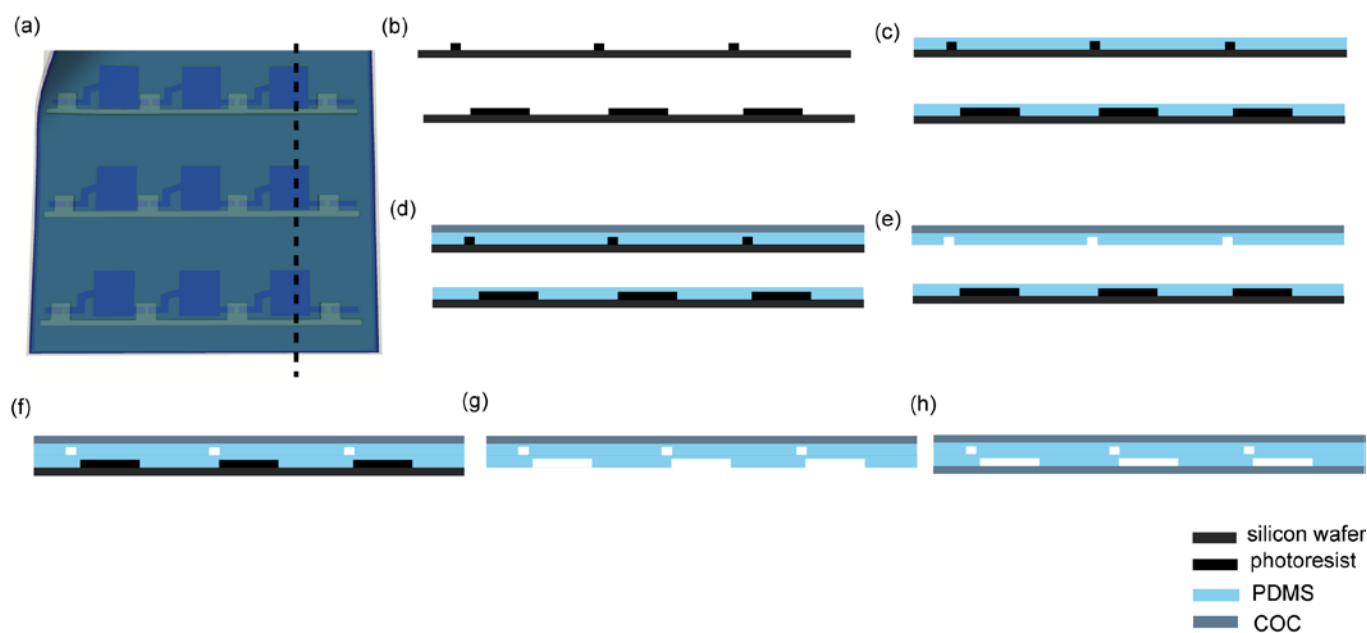


Figure S1. (a) A 3x3 array of single well microfluidic platform. (b-h) Cross-sectional view of chip fabrication.

To fabricate negative photoresist masters (Figure S1b) using SU-8 2050, set a hot plates 65°C and a hot plate to 95°C. Next, obtain two unblemished wafers (which will serve as the control layer and fluid layer masters) and rinse them with acetone and isopropyl alcohol. Dry the wafers using a nitrogen gas dryer, and place them on the 95°C hotplate for at least 2 minutes so that they completely dry. Once the wafers have dried, pour SU-8-2050 on the center of one wafer and lightly drag the mouth of the bottle across the wafer in order prevent the SU-8-2050 from dripping. Place the wafer on a spin-coater and allow it to spin for 35 seconds at 2500RPM for the control layer master. Once this is done, place the newly spun wafer off to the side and repeat the process for the fluid master, setting the spin-coater to

2800RPM. Be sure to keep track of which wafer is the control master and which is the fluid master. Soft bake both masters: 1.5 minutes at 65°C then 6.5 minutes at 95°C, making sure not to cover them with anything. Once they have been baked, remove them from the hot plate and allow them to cool. Pair your mask up with its appropriate master, and one at a time expose them to the UV lamp for 23 seconds, making sure not to place the mask backwards and making sure not to damage the quartz crystal. Next, hard bake the masters: 1.5 minutes at 65°C then 6.5 minutes at 95°C. After they have been hard baked, allow them to cool while the PGMEA baths are prepared. Obtain two glass containers slightly wider than the wafers, and partially fill the containers with PGMEA. Place the masters in their baths and allow them to sit for roughly 5 minutes, while stirring occasionally. After 5 minutes have passed, check to see that all of the photoresist has been dissolved by lightly spraying the wafer with IPA, making sure not to get any IPA into the wafer baths. If a white, clumpy residue forms then there is still photoresist that needs dissolving. Once all of the photoresist has dissolved, wash the wafer with IPA and dry them with nitrogen gas. Finally, silanize the wafers in order to reduce adhesion of the PDMS used in the next stage.

The control layer is made by mixing PDMS and a cross-linker in a 5:1 ratio, and the fluid layer is made by mixing PDMS and a cross-linker in a 15:1 ratio. Stir the PDMS vigorously to ensure a good mixing, and place them under a vacuum pump in order to eliminate the air in the PDMS. Clean the masters using tape to capture any particulate matter or fibers that may have fallen on them during storage. Next, pour the PDMS used for the fluid layers and control layers over the respective masters and remove any bubbles or particulate matter by using a pipette. Spin the fluid layers at 1550rpm for 35 seconds and the control layers at 1150rpm for 35 seconds. Bake the fluid layers and control layers on a hot plate at 80°C, for 12 minutes and 5 minutes respectively. Obtain a sheet of COC and cut out a square slightly larger than the size of the wafer. Remove one of the laminated sides from the COC and place a piece of tape on the still laminated side. Tape the COC to the inside of the plasma cleaner and place the control layer across from the COC so that they are not touching. Allow the plasma cleaner to reach 1500 millitorr before activating the ionized oxygen. Ionize the COC and control layer for 1 minute, then rapidly turn off the plasma cleaner and vacuum, and remove the COC and control layer. Quickly align the COC and control layer and smooth out any bubbles. Bake the combination at 80°C for another 3 minutes, making sure to smooth out any additional bubbles that may form. After baking, peel the COC-control layer combination off of the master, making sure not to let the device rip or be pulled and cause bubbles. Align the COC-control layer sheet with the fluid layer under a microscope, making sure to have the wells match up in the center. The entire device is then baked at 80°C for 5 minutes, and placed in an oven at 60°C overnight. The COC-control layer-fluid layer assembly is then placed on a COC substrate layer.