FORGE NANO
12300 Grant Street, Thornton, CO 80241

Atomic Layer Deposition for Pharmaceutical Powders

Summary

The global pharmaceutical manufacturing market size was valued at $405 billion in 2020 and is expected to grow at a compound annual growth rate of 11.34% from 2021 to 2028.[1] The pharmaceutical industry processes a wide variety of powder materials, from active pharmaceutical ingredients (APIs) to filler materials for use in divided powders. Powders are processed into capsules, tablets, pellets, inhaler doses or ophthalmic treatments such as eye drops. Pharmaceutical powders are predominately organic solids with poor flowability, wettability, compactability, and dispersion, making manufacturing of accurate doses both expensive and time intensive. Biocompatible atomic layer deposition (ALD) coatings can improve flowability, compactability, and particle dispersion enhancing powder processability.

The benefits of ALD layers:

- Improved flowability
- Chemically inert and biocompatible films
- Tunable wettability/dispersibility
- Accelerated *in-vitro* disintegration
- Thermostable storage
- Single-administration doses

Flowability

API powders are frequently in amorphous or hydrate states, which makes manufacturing processing difficult unless the powders are coated.[2] ALD can improve the flowability of powder without chemically changing the bulk particle. In a 2019 study, five TiO_2 ALD layers on the particle surface were enough to quadruple the flowability of a partially crystalline material and to triple the flowability of an amorphous material, yet the coating process did not change the solid form of the materials and did not affect other critical characteristics related to the functionality of the materials.[3]

[1] "Pharmaceutical Manufacturing Market Size Report, 2021-2028." Pharmaceutical Manufacturing Market Size Report, 2021-2028, Grandview Research Reports, July 2021, www.grandviewresearch.com/industry-analysis/pharmaceutical-manufacturing-market.
[2] Sari Airaksinen, Milja Karjalainen, Anna Shevchenko, Sari Westermarck, Ella Leppänen, Jukka Rantanen, Jouko Yliruusi, Role of Water in the Physical Stability of Solid Dosage Formulations, Journal of Pharmaceutical Sciences, Volume 94, Issue 10, 2005, Pages 2147-2165, ISSN 0022-3549, https://doi.org/10.1002/jps.20411
[3] "Improving Powder Characteristics by Surface Modification Using Atomic Layer Deposition" Cosima Hirschberg, Nikolaj Sølvkær Jensen, Johan Boetker, Anders Østergaard Madsen, Tommi O. Kääriäinen, Marja-Leena Kääriäinen, Pekka Hoppu, Steven M. George, et Al, Organic Process Research & Development 2019 23 (11), 2362-2368

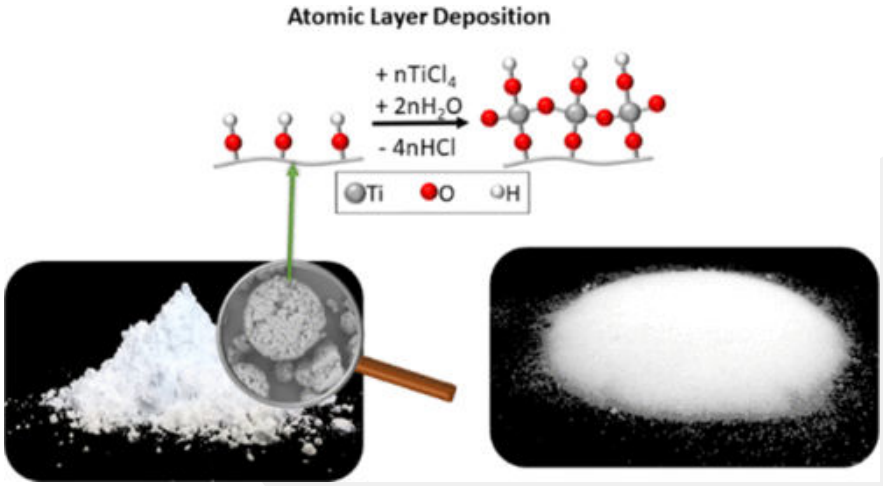

Image 1: Five cycles of TiO_2 ALD performed on powders to quadruple or triple flowability.[3]

Tunable Wettability/Dispersibility

Wettability is a vital characteristic of drug powders as it impacts dispersibility, which is the ability to break down into particles when in contact with body fluids. Tuning the wetting properties of inhaled drug powders have been found to improve bioavailability, increase dispersion, and prevent moisture ingress. ALD and molecular layer deposition (MLD) have been used to tune wettability of drug powders in the spectrum of highly hydrophilic to superhydrophobic. In a study from March 2021, varying ALD chemistries adjusted the water contact angle of budesonide from between 150º and 60º.[4] In a different study from AstraZeneca, ALD was found to effectively modify dispersibility and dissolution rates in as few as 2 – 4 atomic layer cycles.[5]

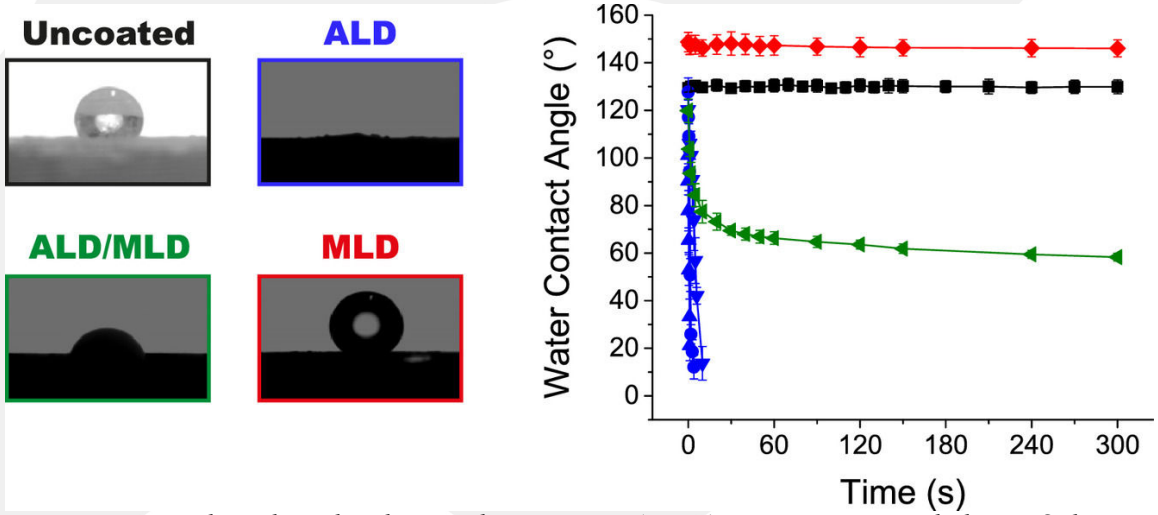

Image 2: Using ALD and molecular layer deposition (MLD) to tune wettability of drug powders.[4]

[4] Damiano La Zara, Fuweng Zhang, Feilong Sun, Maximilian R. Bailey, Michael J. Quayle, Gunilla Petersson, Staffan Folestad, J. Ruud van Ommen, Drug powders with tunable wettability by atomic and molecular layer deposition: From highly hydrophilic to superhydrophobic, Applied Materials Today, Volume 22, 2021, 100945, ISSN 2352-9407, https://doi.org/10.1016/j.apmt.2021.100945

[5] Zhang, D., et al. "Atomic Scale Surface Engineering of Micro- to Nano-Sized Pharmaceutical Particles for Drug Delivery Applications." Nanoscale, vol. 9, no. 32, 2017, pp. 11410–11417., doi:10.1039/c7nr03261g.

Thermostability and Single-Administration

Two components that affect the global distribution of vaccines are the cold-storage requirements and need for multiple doses in the form of "booster shots" in order to maximize vaccine efficacy. In a 2020 study from *Nature - Vaccines*, researchers from the University of Colorado ALD coated HPV vaccine formulations to create thermostable, single-shot vaccines that would otherwise require refrigeration and booster doses.[6] Colorado-based company VitriVax has partnered with Forge Nano for cGMP certified ALD equipment to enable their proprietary Atomic Layering Thermostable Antigen and Adjuvant (ALTA™) technology platform to enable thermostable, single-shot vaccines.[7]

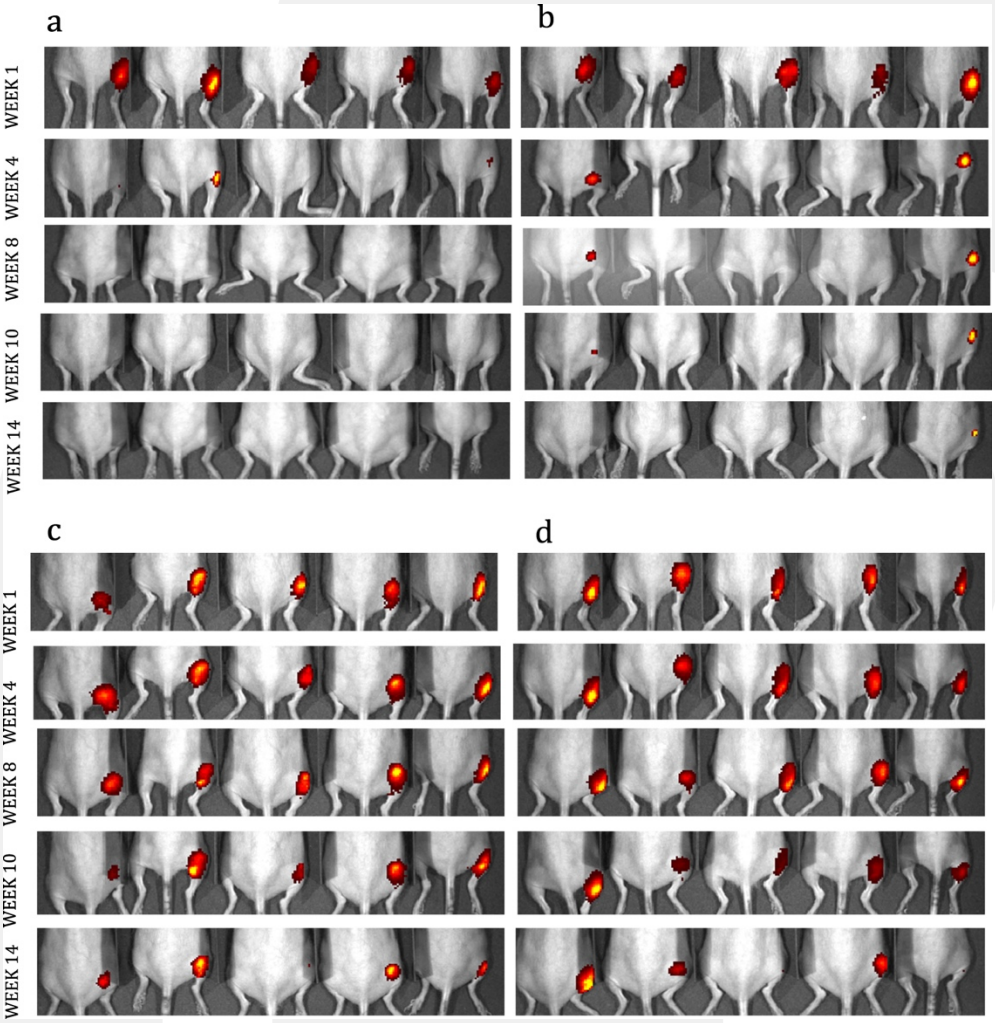

Image 3: Fluorescent images of SKH1 mice recorded at weeks 1, 4, 10 and 14 following injection into their right dorsal thigh with a 5µg of HPV16 L1 that was labeled with IRDye 800CW and adsorbed to alum prior to spray-drying but not coated. b 5µg HPV16 L1 that was labeled with IRDye 800CW, adsorbed on alum, spray-dried and coated with 100 ALD-alumina layers. c 5µg HPV16 L1 that was labeled with IRDye 800CW, adsorbed to alum, spray-dried and coated with 250 ALD-alumina layers, and d 5µg HPV16 L1 that was labeled with IRDye 800CW, adsorbed to alum, spray-dried and coated with 500 ALD-alumina layers.[6]

[6] Garcea, R.L., Meinerz, N.M., Dong, M. et al. Single-administration, thermostable human papillomavirus vaccines prepared with atomic layer deposition technology. npj Vaccines 5, 45 (2020). https://doi.org/10.1038/s41541-020-0195-4

[7] Inc., Forge Nano. "Vaccines Perfected from the Atoms Up." Vaccines Perfected From the Atoms Up, 25 May 2021, www.prnewswire.com/news-releases/vaccines-perfected-from-the-atoms-up-301298733.html.

For more information on using ALD for pharmaceutical powder applications, please contact Tim Porcelli at TPorcelli@forgenano.com.

About Forge Nano
Located just outside of Denver, Colorado, Forge Nano Inc. is the world leader in ultra-thin, surface modification technology for markets including semiconductors, energy storage, catalysis, additive manufacturing, electronic materials, adsorbents, and others. Forge Nano works with strategic partners to jointly develop and integrate ALD-modified materials into commercial supply chains.

Forge Nano's Capabilities

- >20 in-house ALD systems for coating of wafers, powders, and objects
  - Including research, pilot, and commercial scale systems capable of processing anywhere from 1.0 g to 30,000 kg powder per day

- The world's most knowledgeable and experienced team for ALD onto all materials
  - PhD scientists, certified Professional Engineers, career scientists
  - 20+ years' experience designing and building ALD systems

Working with Forge Nano
Forge Nano assists customers daily with both R&D and commercialization of ALD enabled materials. For R&D, we both offer research services for proofs of concept and sell our R&D equipment globally. For commercialization, we offer joint development of products, production equipment, and IP licensing.