RADIO-FREQUENCY-ASSISTED FREEZE DRYING OF PHARMACEUTICAL PRODUCTS: Influence of Applied Power on Drying Time

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Because of the rising demand for lyophilized injectable medicines over the last few decades, particularly in light of the present COVID-19 pandemic, freeze-drying or lyophilization technique has recently received a lot of attention. Freeze-drying is widely used in the pharmaceutical industry because it permits the processing of thermolabile products in sterile conditions, even though it is one of the most time-consuming industrial processes with an efficiency of <10%. To that purpose, RF/microwave-based lyophilization is being pursued because it significantly accelerates such processes. LyoHUB is currently developing a product adaptive RF heating approach to shorten the primary drying process while simultaneously improving the overall batch homogeneity compared with conventional freeze-drying.

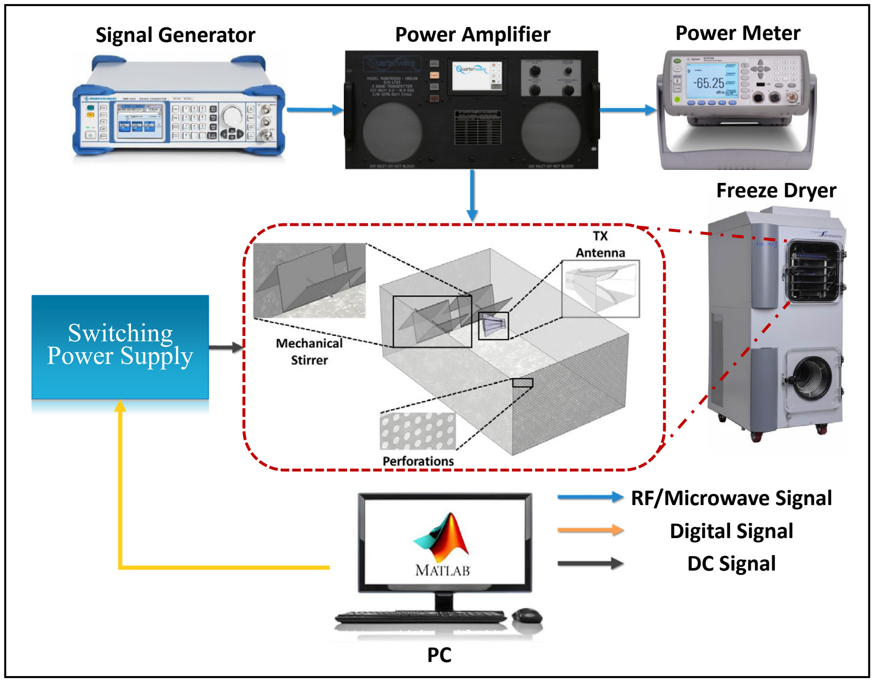

Figure 1: *Block diagram of microwave-assisted lyophilization system.*

Figure 1 depicts the microwave-assisted lyophilization block diagram integrated with a lab-scale lyophilizer. An auxiliary or reverberation chamber (RC), a network analyzer, a power amplifier, an antenna placed inside the RC, and two stepper motors coupled to stirrers inside the RC compose the experimental setup. The RC is a metallic box that houses a transmitting antenna, which serves as a source of RF power inside the chamber. The antenna is connected to a power amplifier to amplify high-frequency (18GHz) electromagnetic signals generated by a signal generator. When the antenna emits electromagnetic waves into the RC, the waves encounter various reflections, resulting in numerous resonances within the chamber. The number of resonances, and thus field uniformity, increases as frequency increases. If the stirrers inside the chamber are fixed, the field distribution stays unchanged, resulting in hot and cold regions inside the RC (highly nonuniform electromagnetic field). To solve this problem, we continually rotate the two stirrers inside the RC to vary the field distribution at different time instants.

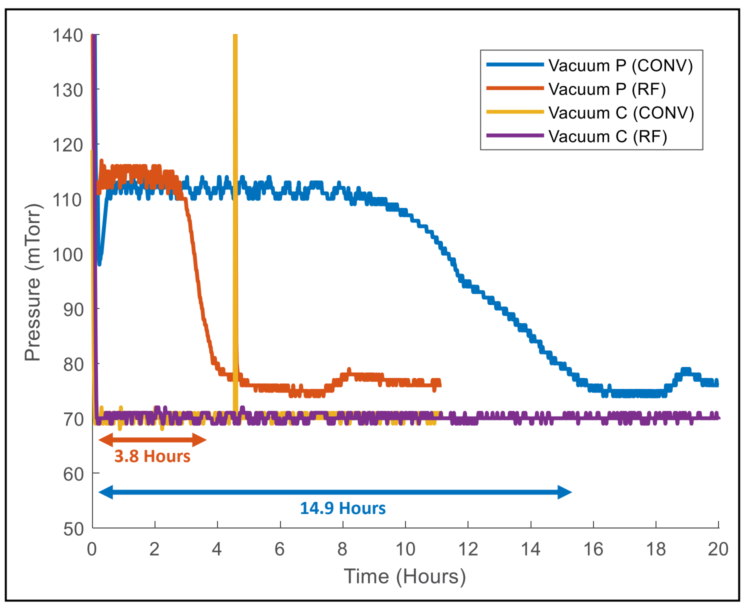

Figure 2: *Capacitance Manometer (CM) and Pirani gauge pressure measurements versus primary drying time for conventional and microwave-assisted lyophilization cycles of sucrose (5% Solids/70% BSA/30% Sucrose), 2R SCHOTT Vial, 0.5 ml fill volume, 60 vials).*

Figure 2 displays the Capacitance Manometer (CM) and Pirani gauge pressure measurements against primary drying time for conventional and RF-assisted lyophilization cycles (BSA with sucrose as excipient).

The primary drying time is reduced from 14.93 hours to 3.9 hours using 40W output RF power (a speedup of 3.8x has been perceived). We have not observed any collapses in the Conventional or the RF-assisted cycles.