Pediatric Gummy Formulations for Drug Resistant Tuberculosis

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Statement of Purpose: Decades of first-line tuberculosis (TB) medication use have led to increasing rates of multi- and extensively drug resistant (MDR/XDR) TB. Adolescent TB represents approximately 20% of the disease burden in low-resource countries, with MDR-TB diagnosed in 25,000 to 32,000 children annually. There are few pediatric-friendly formulations containing second-line TB drugs, and this has resulted in disproportionate effects in children. The limited pediatric options and the need for frequent dose adjustments for growing children during long treatment regimens poses a significant challenge for meeting WHO targets of TB incidence reductions of 90% by 2035. It is therefore imperative that innovative oral formulations of second-line anti-TB drugs be made available to these patients. To address this need, Luna Labs is developing gummy formulations containing anti-TB drugs that are palatable to children and will remain stable for up to two years.

Methods: Second-line anti-TB active pharmaceutical ingredient (API) candidates were evaluated for priority based on availability of pediatric formulations and the clinical needs of current TB treatment regimens. Compatibility between API candidates and expected gummy ingredients was screened, and pectin-based gummies were formulated with down-selected APIs. Gummy taste was iteratively evaluated throughout taste masking and flavoring efforts using assessments of off-notes (e.g., metallic, bitter, mineral) during consumption (e.g., up-front, middle chew, finish, linger). Gummy mechanical properties were also characterized alongside commercially available gummies. For this, a texture profile analysis was performed using an Instron 5943 with double-cyclic compression testing (Figure 1), and key metrics including hardness and chewiness were determined. High performance liquid chromatography (HPLC)/mass spectrometry (MS) methods were established and used to evaluate drug loading, and API stability within the gummy was initially studied through accelerated testing.

Results: Second-line anti-TB medications Moxifloxacin and Clofazimine were selected for the development. Gummies containing each API were successfully formulated using compatible ingredients. At the conclusion of taste-masking efforts, a suitable taste profile was obtained for formulations of each API. Gummy mechanical properties (e.g., hardness, chewiness, resilience) were determined to be comparable to commercially available pediatric gummy vitamins, and the values were below reported maximums of pediatric bite force. API loading was measured to be within the 10% of the of the target API content, and extensive assessments of shelf life are ongoing.

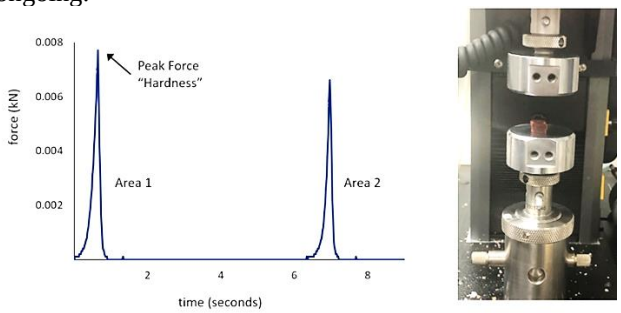

Figure 1. Representative texture profile analysis data (left) obtained through gummy characterization using an Instron 5943 (right).

Conclusions: Second-line anti-TB drugs have been incorporated within palatable, pectin-based gummy formulations. Future work will complete shelf-life assessments and preclinical evaluations, including demonstration of bioequivalence.

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