Research on Synthesizing N-Acetyl-Dl-Leucine for Pharmaceutical Products

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Considering a rising incidence of vertigo disorders in our high school friends (15–40%), this research is aiming for vestibular disease treatment, acetyl-DL-leucin (ADLL, a world-wide therapy). Inspired by classical organic chemistry, ADLL was synthesized and co-crystalized in polyethylene glycol (PEG 6000) for pharmaceuticals. Acylation of L-leucine by acetic anhydride (Ac2O) was conducted, in which reaction conditions (molar ratio, volume, temperature, and scale-up factors) were investigated; data was analyzed using an artificial neural network (ANN). The racemization process was carried out by treating acetyl-L-leucine with Ac2O in presence of NaOH, a unique way for racemize amino acids. Finally, modern techniques (dropping pills and fluid-bed) were employed to co-crystallize ADLL with PEG-6000, resulting a novel drug delivery system for patients. The synthesis process provided ADLL successfully. ANN showed that the Ac2O: L-leucine ratio had a substantial impact on the yield of final product (%); the scaling-up factor, the second-effective factor, could overwhelm issues of volume, temperatures, and purifying conditions. The obtained product was not-only complied with pharmaceutical standards but also equivalent to commercials (assay, polymorphisms, and stability). Finally, the micron-sized ADLL-PEG powder was expected to improve patient compliance when compared to conventional tablets in terms of dose form size, shape, and dissolution profile. Overall, we proposed a batch-technology-based for ADLL synthesis (even at 1 kg scale) that is simple and feasible for implementation worldwide. Finally, this project contributes to the understanding about acylation, racemization, and co-crystallization, aiming for potential pharmaceutical applications.

Awards Won: