Does excipient grade affect the stability of active pharmaceutical ingredients?

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Background: Polysorbate 80 is an excipient often seen in inhaled drug products as a suspension stabilizer. it is also one of the few surfactants approved for pulmonary drug delivery and can be purchased commercially in different grades. Differences occur between grades due to manufacturing and purification processes, handling, storage, and transport conditions. However, these variabilities can impact the degradation of polysorbate 80, which can affect its stabilizing properties, hence the stability of the formulation over time. Therefore, the aim of this work was to determine the effects of polysorbate 80 grade on the physical and chemical stability of budesonide suspension formulations (commercially known as Pulmicort Respules®) used in the treatment of COPD and asthma.

Methods: Budesonide inhalation suspension formulations were prepared containing different grades of polysorbate 80. The formulations were characterized to ensure criteria for inhaled drug delivery were met, i.e., pH in the range 3.5 – 4.8, and particle size in the respirable range of 0.5 – 5 µm. Next, an accelerated stability study was conducted on the formulations by observing changes in the physical characteristics (pH, zeta potential, and particle size distribution) over a storage period of 6 months at 45^{o}C. High pressure liquid chromatography (HPLC) analysis of the formulations plus known degradation products of budesonide was performed to determine chemical stability.

Results: The results showed that the physical characteristics of budesonide inhalation suspension were within optimal specifications for delivery to the lungs. These characteristics remained within acceptable ranges over the stability study period, and the grade of polysorbate 80 did not significantly affect the investigated physical properties. However, significant differences were seen in the formation of the degradation products investigated which varied between the grade of polysorbate 80 used. This study has demonstrated that polysorbate 80 grade may contribute to or protect against the formation of degradation products depending on the chosen degradation product.

Conclusions: In conclusion, considerations should be given to excipient grade choice in combination with knowledge of the degradation pathways the drug product may experience from formulating through its shelf life.