Stability of unit dose preparations of sublingual nitroglycerin tablets in the health system setting

Purpose – Sublingual (SL) nitroglycerin tablets are currently available in glass vials containing 25 or 100 individual tablets. From an inventory control perspective in the inpatient setting, these vials present logistical problems when attempting to store them in automated dispensing cabinets (ADCs) – these vials are frequently misplaced or lost resulting in inaccurate counts and possible delays in therapy. SL nitroglycerin tablets are unique in that the product package insert recommends the tablets should not be removed from the original glass container as the medication can degrade rapidly when exposed to light, humidity, and/or heat. Large scale studies examining tablet stability have not been conducted since the 1980s, it is unclear how current tablet preparations would fare in modern unit dose package preparations. In addition to greater control of inventory, the unit dose packaging of SL nitroglycerin tablets may also reduce costs as a result of fewer tablets purchased. The purpose of our study is to investigate the stability of two SL nitroglycerin products using two different unit-dose packaging methods over the course of 12 months.

Methods – We will evaluate the stability of SL 0.4 mg nitroglycerin tablets in two different unit dose packaging preparations. The first packaging system will utilize the Talyst® JVM Auto Pack Machine, a robotic system that can simultaneously package and apply laser print text to individual dose preparations. This system is efficient and quick but does generate heat. The second system will be a manual process by hand utilizing blister cards; a slower and more time-consuming method but without unnecessary heat. To increase generalizability, two manufacturer products will be tested (Pfizer ([PZR], Greenstone Labs [GSL]). Once prepared, researchers at the University of Kansas School of Pharmacy will perform ultra-performance liquid chromatography with ultraviolet detection (UPLC-UV) for purity testing to assess nitroglycerin tablet content. Prepared study medications will be stored in a Cerner RxStation® automated dispensing cabinet system located within an operational health system pharmacy. Storage compartment humidity and temperature will be recorded three times weekly throughout the study period. These assessments will be conducted on day 0, 30, 90, 180, and 365 after packaging. We expect to observe greater than 90% stability relative to the reference standard through a one-year study period in at least one packaging preparation.

Results – Research in Progress. A UPLC-UV method was developed using a certified nitroglycerin reference standard to create a 5-point calibration curve from 25% to 125% resulting in an average coefficient of variation of 2.5%. Following extraction nitroglycerin content was measured by interpolation on the resulting linear standard curve (r^2=0.9997). A forced degradation experiment was performed by placing tablets at 50°C in an open container and resulted in a 48% loss of potency over 43 hours. Day 0 analysis was complete with 99 +/- 2.2% and 100 +/- 3.2% potency for the PZR and GSL products, respectively. Day 0 storage compartment humidity and temperature was 31% and 76.6°F, respectively. Projected completion: March 2022

Conclusions - Research in Progress

Matt H Bilhimer Pharm.D., BCPS Clinical Pharmacist – Emergency Medicine & Critical Care Olathe Medical Center Olathe KS	Yezan M Salamoun Pharm.D. Candidate 2023 University of Kansas School of Pharmacy Lawrence KS	Phil J Schneider Director of Pharmacy Olathe Medical Center Olathe KS	James M Backes Pharm.D. Associate Dean for Clinical and Medical Center Affairs Assistant Director Atherosclerosis and LDL-Apheresis Center Professor – University of Kansas School of Pharmacy	Ryan Funk, Pharm.D., Ph.D Associate Professor and Associate Chair Department of Pharmacy Practice University of Kansas Medical Center 3901 Rainbow Blvd, 4073 HLSIC Kansas City KS