**Thesis Title** The Development of Phenylpropanolamine Hydrochloride Extended-Release Capsules using Thermosoftening Vehicle.

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## ABSTRACT

Liquid filled hard gelatin capsules were explored as a potential extended release delivery system. Phenylpropanolamine hydrochloride (PPA) was used as a model drug and a series of thermosetting fatty vehicles (Gelucires®) with varing HLB values and melting points were used as excipients. The drug and vehicle were molten together at lowest temperature possible and filled in a stainless steel die with an upper planar surface exposed to the dissolution medium. The intrinsic release of PPA was studied using the die immersed in one liter beaker with constant speed stirring at 100 rpm at $37^{o}$ C. It was found that increasing the ratio of PPA to Gelucire® from 15:100 w/w to 30:100 w/w, the release rate was increased by about 2 fold. The HLB value of the vehicle played important role in release kinetics rather than its melting point. The release profile fitted better to matrix type as described by Higuchi's model. Differential scanning calorimetry study had shown no interaction between the drug and excipients.

An inert wax type extended release capsules of phenylpropanolamine hydrochloride was developed. The required release characteristic was calculated

from the pharmacokinetic parameters of the drug. A total dose of 75 mg PPA with the release rate of 9 to 13 $mg/cm^2/hr^{1/2}$ over 8 hours period is required. The drug was incorporated with Gelucires® and filled in capsules. The dissolution profile of the capsules were studied using USP Apparatus 1(USP XXII method). It was found that Gelucire 50/13 containing 15:100 w/w of the drug conforms to USP requirements on the monograph of the extended release PPA capsules. The stability of the PPA extended release capsule was studied at ambient and accelerated conditions. It was found that the dissolution profile, DSC thermogram and drug content were not significantly different after 3 months of storage at ambient conditions. Nevertheless storage of this formulation under accelerated conditions ($40^oC$, 75% RH) displayed a significant influence on the dissolution behavior.