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Formulation and in Vitro/ in Situ Evaluation of Gel Matrix System for  
Sustaining the Release of Paracetamol

By

Ruaa Thaer Abdulsalam Al-Ajeeli

A thesis Submitted in  
Partial Fulfillment of the  
Requirements for the Degree of  
Master of Science  
In Pharmaceutical Sciences

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Amman-Jordan  
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Signature

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## Abstract

### Formulation and in Vitro/ in Situ Evaluation of Gel Matrix System for Sustaining the Release of Paracetamol

By

Ruaa Thaer Abdulsalam Al-Ajeeli

Petra University, 2010

Under the supervision of Dr. Riad Awad and Dr. Faisal Al- Akayleh

Development of sustained release oral dosage forms is beneficial for optimal therapy regarding the efficacy, safety and patient compliance. Frequently used approaches to achieve adequate control of drug release include combination of hydrophilic and lipophilic excipients. The present work studied the potential use of three low melting point highly hydrophobic grades of Gelucire<sup>®</sup> (G43/01, G39/01 and G33/01) and sodium alginate (SA) – Chitosan (CH) to prepare sustained release prototype gel preparation.

Paracetamol (PA, the model drug) was first dispersed in a molten Gelucire<sup>®</sup> base which was added to sodium alginate-chitosan polymeric phase with homogenization. Two gel ratios were prepared (PA : G : SA-CH, 1:1:4 and 1:1:8) using three different concentration of Sodium Alginate-Chitosan polymeric phase 3-3%, 4.5-4.5% and 6-6%.

Effect of formulation variables including SA and CH concentration, polymeric phase ratio and Gelucire<sup>®</sup> type and ratio on the release behavior were studied. The formed prototype gels have the ability to form gel-matrices instantaneously in acidic fluid as a result of sodium alginate conversion into alginic acid. In vitro pH–gradient release

studies indicated that the preparation with prolong release characteristics is feasible for up to 8 hr.

The incorporation of CH to SA resulted in a smooth controlled release pattern and absence of the biphasic release pattern observed with SA alone as a result of alginate erosion at higher pH media. Polyelectrolyte complex between CH and SA is expected to play a role in the controlling process at pHs 5.4 to 6.8. Further, the incorporation of Gelucire® to the SA-CH polymeric phase caused an increased in the matrix lipophilicity and the formation of more rigid gel-matrix with higher ability to retard drug release. The release behavior had been proved to be highly dependent on the gel-matrix composition.

Kinetic analysis of the prepared gels showed predominantly diffusion control release mechanism with slow erosion.

The studied formulas showed a pseudo-plastic rheological behavior and viscosity directly proportional with melting point of Gelucire®

On the basis of the differential scanning calorimetric analysis results, Paracetamol were found to be compatible with Gelucire®.

The preliminary in situ evaluation in rats had demonstrated the feasibility of forming gel-matrix with sufficient integrity in the stomach following oral administration similar to that formed in vitro.

Major Supervisor Signature

Dr. Riad Awad



*To*  
*My Family.....*