

**UNIVERSITI TEKNOLOGI MARA**

**pH-SENSITIVE NANOPARTICLES AS CARRIERS  
FOR ORAL DELIVERY OF A MODEL  
PEPTIDOMIMETIC DRUG**

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## DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any other degree or qualification.

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## ABSTRACT

Peptide-related drugs are usually unstable in the harsh gastrointestinal environment with poor absorption throughout the gut. The potential of anionic pH-sensitive nanoparticles to act as novel drug carriers for oral administration of such compounds was investigated using a peptidomimetic drug, cefotaxime sodium.

Drug loaded nanoparticles were prepared using a pH-controlled nanoprecipitation method. Three types of nanoparticles were prepared using different grades of Eudragit polymer, namely L100, L100-55 and S100. The drug-loaded nanoparticles have a size of about 100 nm, low polydispersity, encapsulation efficiencies of more than 50%, drug entrapment and drug content between 4-5%.

Bioavailability studies were initially conducted in rats according to a crossover design. However, a carry-over effect was observed with visible reduction of cefotaxime absorption following the first exposure of the rats to the drug-loaded nanoparticles. This phenomenon was confirmed with repeated administration of the same drug-loaded nanoparticles to the same rats (after one week wash-out period). Thus, in subsequent studies, a parallel group design was used instead. The extent of cefotaxime bioavailability was found to increase in the following order with the different polymeric nanoparticles: S100>L100-55>L100.

Bioavailability of the nanoparticles from isolated segments of rat intestines was further investigated to determine if they were preferentially absorbed from specific regions. Absorption was found to occur in the entire small intestine. However, the duodenum, jejunum and jejunum-ileum areas were observed to be the optimal sites for absorption of the L100, L100-55, and S100 nanoparticles respectively.

Finally, the drug-loaded nanoparticles were also observed to enhance the lymphatic transport of the contained drug. The ratio of the cefotaxime concentration in the lymph over that of the plasma obtained with administration of the nanoparticles was consistently higher than that obtained with administration of an aqueous solution of the drug, suggesting that nanoparticles could promote the lymphatic transport of the drug.

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