J. Pharm. Pharmacol. 1998, 50 (Supplement): 143

Gut transit of PLGA nanoparticles following a single oral dosing

V. ADEKOYA, J. T. TURTON AND A. T. FLORENCE

Centre for Drug Delivery Research, The School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX

Particle parameters (e.g. density, or surface properties) do not affect gastric emptying (Gruber, et.al. 1987) but liquids and small solids (< 1 mm) have been shown to leave the stomach quickly especially during fasting (Lin, et.al. 1992). Few studies however have been carried out on the gut transit of nanoparticles. To achieve absorption via the oral route from nanoparticles, the carriers not only have to survive the harsh conditions of the gut, but also have to have significant residence time within the GI tract at the site of uptake (small and large intestine) if translocation across the epithelial barrier is to be achieved.

he gastrointestinal transit of 200 nm diameter poly (lactide co-glycolic acid) (PLGA) nanoparticles (222 nm) (with I^{125}-salmon calcitonin (I^{125}-sCT) entrapped as a tracer) was monitored. Loaded particles were administered as an aqueous suspension to one group (n=3) of overnight fasted male Wistar rats. At various time intervals, sections of the gut were removed and the contents washed to determine the levels of radioactivity. Low levels (2.5%) of PLGA particles were detected both in stomach tissue and stomach contents 4h after dosing (Fig. 1)

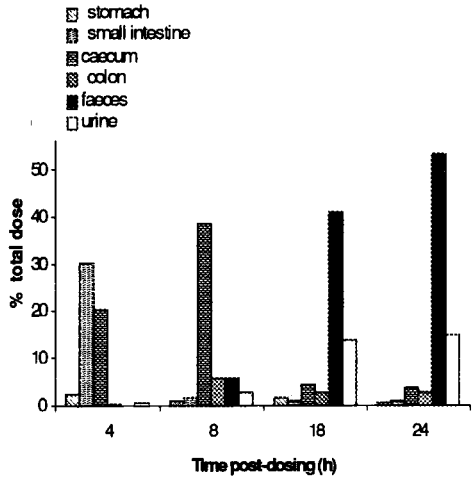

Figure 1: Levels of radioactivity in gut (includes contents) and urine following oral gavage of I^{125}-sCT-loaded PLGA 56:44 nanoparticles suspension in rats (n=3).

indicating rapid gastric emptying. In the small intestine, 30% particles was detected at 4h (of which 3.7% was present in the tissue). This total content load had decreased to about 2% at 8h. In the caecum, 20% and about 40% of the particle dose was detected at 4 and 8 h respectively, and 53% was detected in faeces at 24 h. The short residence time of nanoparticles in the gut may explain in part the small percent of total dose of nanoparticles absorbed from the gut, a major proportion ending up in faeces.

These results are in accordance with those reported for the gastric emptying of liquids and indigestible solids (Kelly, 1980). We have previously shown our PLGA particles to be stable in simulated gut fluids after 24h incubation (Adekoya & Florence, 1997). Orally administered peptide drugs have very low bioavailability due to enzymatic degradation in the gut milieu, but entrapping the drug within nanoparticles offered protection to the drug. For significant absorption of intact PLGA nanoparticles to be achieved via lymphoid and nonlymphoid tissues, the residence time and interaction with those absorption sites tissues has to be enhanced.

References

- Adekoya, V. and A.T. Florence, (1997) Pharm. Res., 14: S-716.
- Gruber, J. Rubinstein, A., Li, V.H.H., Bass, P., and Robinson, J.R., (1987) J. Pharm. Sci., 76: 117-122.
- Kelly, K.A., (1980) Am. J. Physiol., 239: G71-G76
- Lin, H.C., Elashoff, J.D., Guy, Y.G., Meyer, J.H., (1992) J. Gastroint. Mot., 4: 157 – 163.

Acknowledgment: VA thanks Novartis for sponsorship in part.