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The effect of polyethylene glycol 400 (PEG 400) on gastrointestinal transit

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Poorly water-soluble drugs usually exhibit low oral bioavailabilities as a consequence of limited dissolution within the gastrointestinal tract. Such drugs can be solubilised using PEG 400 and then presented as liquid formulations, thereby overcoming the dissolution and bioavailability problems. Although this approach has been used with some success, in some cases the results have been unpredictable. The bioavailability of griseofulvin, for example, was considerably lower from a PEG 400 solution than a conventional hard gelatin capsule containing pure drug powder (Hansford et al, 1980). This apparent anomaly was thought to be related to possible differences in gastrointestinal transit of the two formulations. However, further work was not conducted to verify the afore mentioned hypothesis. Hence, the purpose of the present study was to investigate whether PEG 400 has any effect on gastrointestinal transit.

Ten healthy male volunteers participated in the study, after providing written informed consent and adherence to an overnight fast. Two days of study, at least one week apart, were completed by each volunteer, the type of administration varying on each occasion. The first administration consisted of 150 ml of orange juice (osmolarity, 606 mOsm) [OJ], whereas on the second occasion the volunteers received 150 ml of orange juice containing 10 g of PEG 400 (osmolarity, 951 mOsm) [OJ + PEG 400]. The drinks were radiolabelled with 2.5 MBq of ^{111}In-DTPA to allow their position *in vivo* to be monitored using a double-headed gamma camera. Simultaneous anterior and posterior scintigraphic images of 30 seconds duration were acquired every 5 minutes until the drink had emptied from the stomach, and then at 10 minute intervals until the radioactivity had reached the colon. The data was analysed quantitatively by creating regions of interest around the stomach and colon. The counts in each region were corrected for background radiation and decay, prior to calculation of the geometric mean. Plots of gastric emptying and colon arrival curves were then used to estimate t_{50} values for both processes, with the difference between the two representing small intestinal transit time.

Table 1. Gastrointestinal transit times (Mean ± SD).

Administration	GET (min)	SITT (min)	CAT (min)
OJ	12 ± 3	203 ± 52	215 ± 54
OJ + PEG 400	17 ± 3	124 ± 39	141 ± 38

GET = Gastric emptying time
SITT = Small intestinal transit time
CAT = Colonic arrival time

As can be seen from Table 1, there was a slight difference in the gastric emptying times between the two administrations ($p < 0.05$). In addition, there was an even greater difference in colonic arrival times ($p < 0.01$), as a result of differential small intestinal transit ($p < 0.01$). These results clearly demonstrate that PEG 400 has a profound effect on small intestinal transit, resulting in a 39% reduction in transit time. The reason for this effect is probably related to the hypertonic nature of PEG 400 which, after administration, is likely to hold or draw fluid into the intestinal lumen, thereby increasing bulk volume, stimulating peristalsis and resulting in a decrease in transit time.

Overall, these findings have important implications with regard to the formulation of poorly water-soluble drugs with PEG 400. Not only will such an approach improve drug solubility, but the concurrent reduction in gastrointestinal transit time may limit the opportunity for drug absorption and nullify any possible bioavailability enhancement!

Hansford D.T., Newton J.M. and Wilson C.G. (1980) Pharm. Ind. 42 (6) 646-650