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An in-vitro investigation into the effect of fatty foods on drug release from a polysaccharide based controlled release dosage form

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Food effects studies can have great importance in providing information on dosing strategies in the fed and fasted states. Such an understanding can help to form selection criteria aimed at developing a drug product with minimised variability in bioavailability. Food effect studies on controlled release formulations are more critical because the influences on bioavailability by food are not only dependent on the drug but also on the components of the dosage form.

The present study was to particularly examine the effect of a simulated high-fat meal on a hydrophilic controlled release tablet of propranolol hydrochloride (PLHCL) using an *in vitro* model similar to that described by Esbelin (1991). These results were compared with those obtained from a commercial sustained release dosage form of propranolol-Inderal LA. The model utilises peanut oil as a simulated fatty food component, by soaking the dosage form in the oil prior to the dissolution test. PLHCL (50) mg was incorporated into 450mg TIMERx matrix directly compressed. Drug release was determined using USP XXIII type 3 Bio-dis dissolution apparatus (Caleva Instruments, Sturminster Newton, UK). The test was carried out in 250ml dissolution medium, with dipping speed-20dpm, at 37°C. The pH of dissolution media and time intervals were pH1.2 for 1hr, pH 2.5 for 1hr, pH4.5 for 4 hrs, pH6.8 for 4hrs and pH 7.5 for 14 hrs. Dosage forms were treated by agitation in peanut oil for 2 hrs at 37°C. In the case of Inderal LA, the beads from capsules were directly placed into the oil. The amount of PLHCL released in dissolution media was analysed at 288nm using UV spectrophotometry. Dissolution tests on dosage forms without oil-treatment were conducted under the same conditions.

The results (fig.1) shows that drug release profile from the TIMERx tablet was not significantly influenced by peanut oil treatment, though 8-9% (w/w) oil was adsorbed onto the tablet. By contrast, drug release from oil-treated Inderal LA beads was significantly decreased, with ~50% reduction in drug release over the first six hours.

The effect of the oil on the Inderal system was attributed to the ethylcellulose film on the beads, the oil coating potentiating its hydrophobicity, therefore blocking the pathway of drug release. TIMERx matrix components are hydrophilic, so that the oil almost exerts no impact on the swelling of the dosage form, and consequently does not alter the drug diffusion pathway.

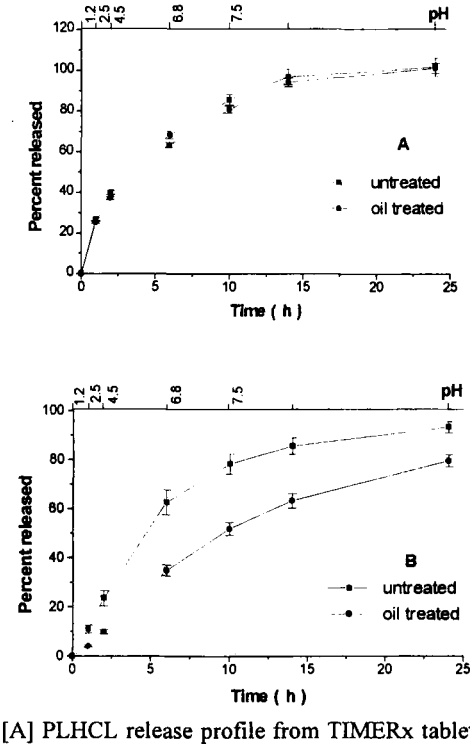

fig 1: [A] PLHCL release profile from TIMERx tablets (n=6) [B] PLHCL release profile from Inderal LA capsules (n=6)

Esbelin, B et al (1991) J. Pharm. Sci. 80:991-994