Predicting Blood Drug Concentration-Time (C-T) Profiles Using Convolution Technique - Valproic Acid

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A new approach, based on the convolution technique, using spreadsheet software, such as MS Excel, has been suggested to predict blood drug conc.-time (C-t) profiles (link). The technique provides a simple approach in linking drug dissolution results to blood drug levels in humans. Examples of its use and validations have been described earlier (link). This article provides another application of the convolution technique for a sustained-release (SR) valproic acid product.

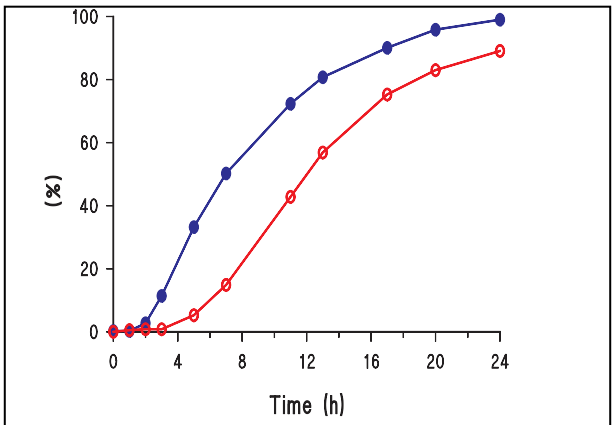

Figure 1: Drug dissolution profiles of two valproic acid products as described in the publication. See text for details.

The drug dissolution data used in this article to predict C-t profiles is obtained from a publication and is redrawn in Figure 1. [Fujii *et al,* Comparative in vivo bioequivalence and in vitro dissolution of two valproic acid sustained-release formulations. Drug Design, Development and Therapy 2008:2 139–144.]

The publication also provides in vivo data i.e., bioavailability results thus facilitating the usefulness in validation of the convolution technique. To predict the C-t profiles, the required pharmacokinetic (PK) values used are taken from here (link).

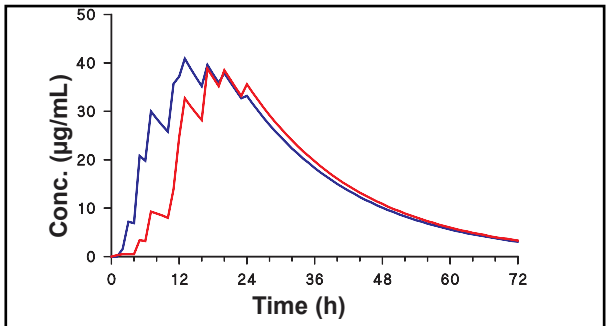

Figure 2: Predicted C-t profiles based on drug dissolution characteristics of two valproic acid products as shown in Figure 1.

The predicted C-t profiles of the two SR products are shown in Figure 2. The predicted values of the PK parameters (C_{max}, t_{max} and AUC) and the corresponding reported values from the bioavailability study are summarized in Table 1 below.

It is evident that the convolution technique predicted the C-t profiles and associated PK parameters well, as in the cases described earlier. Therefore, this article provides further evidence in support of the general use of the suggested convolution technique.

Table 1: PK parameter values derived from the predicted C-t profiles shown in Figure 2.

Product	%Dissolution at 24h	C_{max} (µg/mL)	AUC (µg.h/mL)	C_{max} (h)	AUC (µg.h/mL)
Results as reported in the publication from bioavailability study					
REF	99	42.4	1361		
TEST	89	40.9	1458		
Values obtained from the predicted C-t profiles					
REF		40.9	1272	41.3‡	1285‡
TEST		38.9	1128	44.7‡	1267‡
‡Normalized to 100% dissolution					