# Development of Etoricoxib Cubosomal Transdermal Gel as An Alternative to Systemic Administration

## 1. METHODOLOGY

### 1.1. Construction of calibration curve of Et in in different media

Calibration curves of Et were constructed in pH 6.4 phosphate buffer solution and methanol. From the previously prepared standard stock solutions of Et in pH 6.4 phosphate buffer solution and methanol, serial dilutions with pH 6.4 phosphate buffer solution and methanol were made separately to obtain solutions having concentrations ranging from 3 µg/mL to 10 µg/mL. The absorbances of these solutions were measured spectrophotometrically at wavelength of 235 nm against pH 6.4 phosphate buffer solution and methanol respectively as blank. The experiments were carried out in triplicate.

## 2. RESULTS and DISCUSSION

### 2.1. Calibration curve of Et in different media

At the predetermined $\lambda_{max}$ of 235 nm, the absorbance values for the calibration curves of Et in both pH 6.4 phosphate buffer solution and methanol were obtained. Concentration-absorbance graphs were plotted for each medium (Figure 2a for pH 6.4 phosphate buffer solution and Figure 2b for methanol). The results demonstrate that Et adheres to Beer's Lambert Law within the tested concentration ranges at the $\lambda_{max}$ of 235 nm. As shown in Figure 2a and Figure 2b, the correlation coefficients ($R^2$) were found to be approximately 0.9969 for pH 6.4 phosphate buffer solution and 0.9939 for methanol, indicating excellent linearity in both cases.

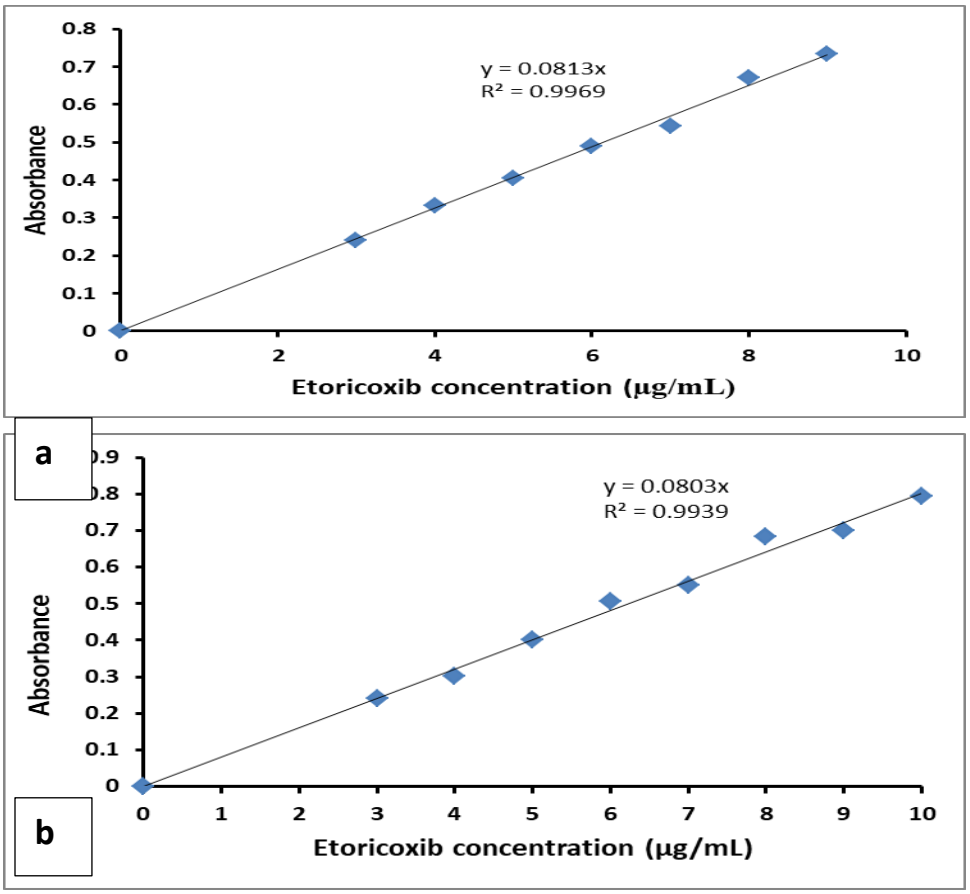


**Figure 1S.** Calibration curve of Et (a) in pH 6.4 phosphate buffer solution and (b) in methanol at $\lambda_{max}$ 235 nm .

**Table 1S.** kinetic parameters calculated for the dissolution data of Etoricoxib from Etoricoxib -loaded cubosomal dispersions (S1- S9).

| Formulation | Zero order | | First order | | Diffusion (Higuchi) | |
|---|---|---|---|---|---|---|
| | r | k | r | k | r | k |
| **S1** | 0.95677 | 0.16071 | 0.61693 | 0.49188 | **0.99551** | 0.42977 |
| **S2** | 0.93522 | 0.15692 | 0.61147 | 0.49192 | **0.99492** | 0.42907 |
| **S3** | 0.88841 | 0.15321 | 0.61159 | 0.49195 | **0.97948** | 0.43455 |
| **S4** | 0.97578 | 0.15321 | 0.61137 | 0.49195 | **0.99289** | 0.40068 |
| **S5** | 0.95580 | 0.15778 | 0.61140 | 0.49191 | **0.99649** | 0.42279 |
| **S6** | 0.93791 | 0.15750 | 0.61145 | 0.49191 | **0.99649** | 0.42948 |
| **S7** | 0.98736 | 0.15250 | 0.61132 | 0.49196 | **0.98524** | 0.39110 |
| **S8** | 0.97884 | 0.15875 | 0.61132 | 0.49190 | **0.99431** | 0.41446 |
| **S9** | 0.96469 | 0.15535 | 0.61140 | 0.49193 | **0.99870** | 0.41336 |

**Table 2S.** kinetic parameters calculated for the dissolution data of Etoricoxib from Etoricoxib cubosomal gel formulations (G1- G6).

| Formulation | Zero order | | First order | | Diffusion (Higuchi) | |
|---|---|---|---|---|---|---|
| | r | k | r | k | r | k |
| **G1** | 0.910392 | 0.038318 | 0.326007 | 0.068387 | **0.992577** | 0.215397 |
| **G2** | 0.86587 | 0.037164 | 0.326103 | 0.068398 | **0.982914** | 0.217514 |
| **G3** | 0.864426 | 0.037522 | 0.326087 | 0.068395 | **0.980074** | 0.219344 |
| **G4** | 0.952613 | 0.039857 | 0.325801 | 0.068372 | **0.99496** | 0.196755 |
| **G5** | 0.966092 | 0.038719 | 0.325922 | 0.068383 | **0.984438** | 0.203425 |
| **G6** | 0.908281 | 0.039059 | 0.32597 | 0.068379 | **0.98907** | 0.219296 |

**Table 3S.** Permeation kinetics of Et gel and Et cubosomal gel (G3).

| Formulation | $r^2$ | JS steady-state flux ($\mu g\ cm^{-2}\ hr^{-1}$) | P permeability coefficient ($cm\ hr^{-1}$) |
|---|---|---|---|
| **Et gel** | 0.9552 | 4.361 | 0.0043 |
| **Et cubosomal gel (G3)** | 0.8756 | 4.507 | 0.0045 |