

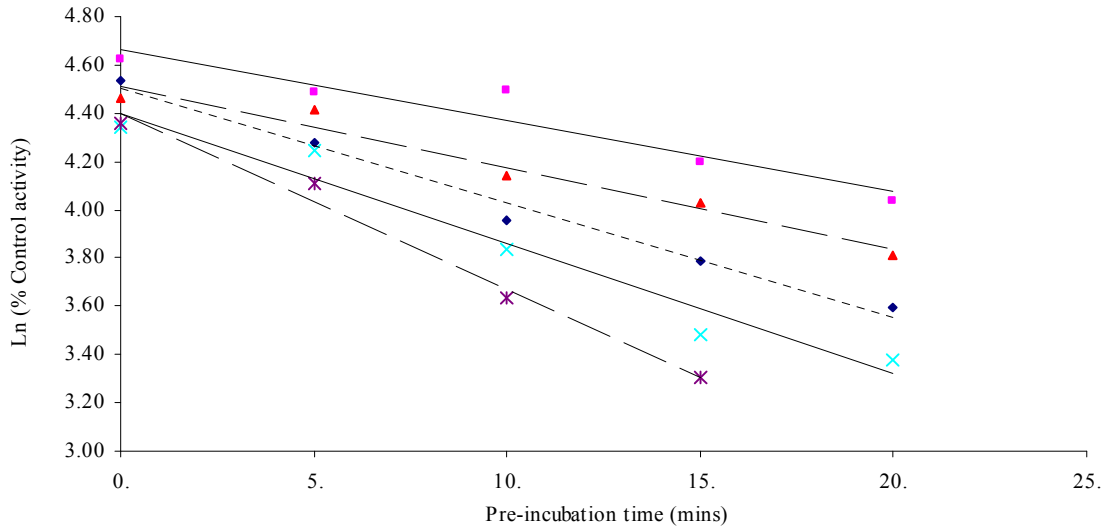


## Mechanism Based Inhibition (Irreversible Inhibition)

P450	Model substrate	Metabolite	Model inhibitor	Assay
CYP1A	7-Ethoxyresorufin	O-deethyl-7-hydroxyresorufin	Furafylline	Fluorimetric
CYP1A1	Phenacetin	Acetaminophen	Furafylline	HPLC-MS/MS
CYP2A6	Coumarin	7-hydroxycoumarin	Methoxsalen	Fluorimetric
CYP2C8	Paclitaxel	6 $\alpha$ -Hydroxypaclitaxel	Isoniazid	HPLC-UV
CYP2C9	Tolbutamide	4-Hydroxytolbutamide	Tienilic acid	HPLC-MS/MS
CYP2C19	S_Mephenytoin	4-Hydroxymephenytoin	Ticlopidine	HPLC-MS/MS
CYP2D6	Bufuralol	1'-Hydroxybufuralol	Paroxetine	HPLC-fluorimetric
CYP2E1	Chlorzoxazone	6-hydroxychlorzoxazone	DDC	HPLC-UV
CYP3A	Testosterone	6 $\beta$ -hydroxytestosterone	TAO	HPLC-radiodetection
CYP3A	Midazolam	1-hydroxymidazolam	TAO, Erythromycin, Verapamil	HPLC-MS/MS

### Determination of $K_{inact}$ and $K_I$ for furafylline against CYP1A2 (phenacetin O-deethylase) activity

ln % residual activity



■ 1  $\mu$ M

▲ 2.5  $\mu$ M

◆ 5  $\mu$ M

× 10  $\mu$ M

✖ 15  $\mu$ M

$$y = -0.0293x + 4.66$$

$$R^2 = 0.916$$

$$y = -0.0338x + 4.51$$

$$R^2 = 0.966$$

$$y = -0.0474x + 4.50$$

$$R^2 = 0.986$$

$$y = -0.0536x + 4.39$$

$$R^2 = 0.958$$

$$y = -0.0731x + 4.40$$

$$R^2 = 0.988$$