

# Carboxylesterase (CE) Inhibition

## Background Information



'CE inhibitors potentially have dual roles in modulating drug action, by both reducing induced toxicity and/or increasing molecule half-life.'

<sup>1</sup>Hatfield M.J. and Potter P.M. (2011) *Expert Opin Ther Pat* **21(8)**; 1159-1171

- Human carboxylesterases (CE) are Phase I drug metabolising enzymes of the serine hydrolase superfamily. They hydrolyse a variety of ester containing drugs and prodrugs.
- Carboxylesterase inhibitors may play a role in improved efficacy of compounds inactivated by this class of enzymes and/or reduce the toxicity of agents that are activated by these enzymes.
- Cyprotex's carboxylesterase inhibition assay identifies if your compound is an inhibitor of the carboxylesterase (CE) isoforms, hCE1, using hCE1-b and hCE1-c recombinant enzymes.

### Protocol

#### Test System

hCE1-b and/or hCE1-c expressed enzymes

#### Substrates

Trandolapril (hCE1)

#### Metabolites

Trandolaprilat (hCE1)

#### Test Article Concentrations

0, 0.4, 1, 4, 10, 40 and 100  $\mu$ M (different concentrations available)

#### Positive Control Inhibitors

Benzil (hCE1)

#### Test Article Requirements

100  $\mu$ L of a 40 mM DMSO solution (or equivalent amount in solid)

#### Analysis Method

LC-MS/MS

#### Data Delivery

IC<sub>50</sub>

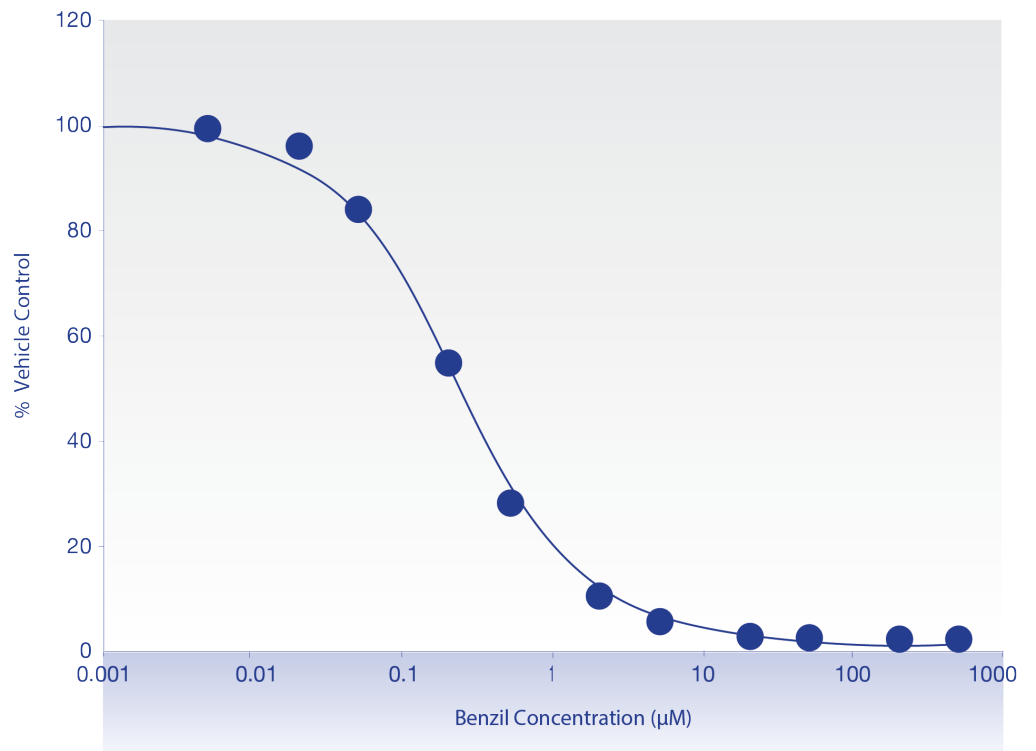
Standard error of IC<sub>50</sub>

% Control at each concentration

'modulation of CE activity may present an opportunity to alter drug metabolism and pharmacokinetics, with the ultimate goal of improving therapy.'<sup>1</sup>

**Figure 1**

Inhibition of trandolapril (hCE1 substrate) metabolism in recombinant hCE1-b by benzil.



**References**

<sup>1</sup> Hatfield M.J. and Potter P.M. (2011) *Expert Opin Ther Pat* **21**(8);1159-1171