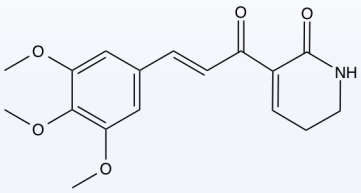
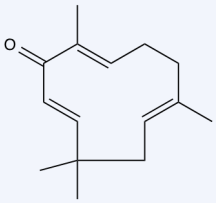
FOCUS on...

Glutathione Homeostasis



Piperlongumine



Zerumbone

Glutathione (GSH) homeostasis plays a role in both cancer prevention and progression. GSH scavenges cellular ROS, RNS and electrophiles under stress conditions preventing tumor initiation.1 Conversely, this scavenging ability of GSH becomes a liability once a cell becomes cancerous enabling it to survive.1,2 GSH is important for the maintenance of intracellular redox balance and the essential thiol status of proteins – critical for cancer cells that typically exist in an enhanced cellular stress environment.3 GSH can conjugate to chemotherapeutics resulting in their efflux from cells via the glutathione S-conjugate complex export protein (GS-X pump) resulting in acquired drug resistance.4,5 In addition, maintenance of high levels of GSH may be critical for the extravascular growth of metastatic cells.6 The specific targeting of cancer cells via their dependence on the stress response pathway is an exciting and cutting edge area of cancer research.

Piperlongumine

Piperlongumine is a natural product isolated from the plant *Piper longum*. It selectively increases reactive oxygen species (ROS) and apoptosis in cancer cells via inhibition of glutathione S-transferase pi and reduction of glutathione. In addition, it potently inhibits spontaneously formed malignant breast tumor growth and associated malignancies in mice.[7]

10-2377 20 mg , 100 mg

Zerumbone

Induces apoptosis in HCT116 colon cancer cells via induction of TRAIL death receptors 4 and 5. This induction was abolished by glutathione suggested a critical role for ROS.[8] Zerumbone mediated apoptosis has been shown to be selective for cancer cells.[9] Recent work has implicated calpain and ROS-mediated BAX activation for zerumbone's activity.[10]

10-2247 10 mg , 50 mg

Carnosic Acid

Anti-oxidant and cancer chemoprotectant that acts via induction of glutathione S-transferase and increase of glutathione levels.[11,12]

10-2401 10mg , 50 mg

Dehydrozingerone

A natural constituent of ginger that inhibited the growth of HT-29 human colon cancer cells *via* accumulation of intracellular ROS.[13]

10-2526 1 mg , 5 mg

CAPE

Selective inhibitor of glutathione S-transferase in the presense of tyrosinase.[14] Selective inhibition of the growth of human lung cancer A549 cells by CAPE was attributed to the depletion of cellular glutathione.[15]

10-2265 10 mg , 50 mg

References:

1. Balendiran *et al.* (2004) Cell.Biochem.Funct. **22** 343
2. Cabello *et al.* (2007) Curr.Opin.Investig.Drugs **8** 1022
3. Townsend *et al.* (2003) Biomed.Pharmacother. **57** 145
4. Godwin *et al.* (1992) PNAS **89** 3070
5. Mulcahy *et al.* (1994) Mol.Pharmacol. **46** 909
6. Estrela *et al.* (2006) Crit.Rev.Clin.Lab.Sci. **43** 143
7. Raj *et al.* (2011) Nature **475(**7355**)** 231
8. Yodkeeree *et al.* (2009) Cancer Res. **69** 6581
9. Xian *et al.* (2007) Cancer Sci. **98** 118
10. Sobhan *et al.* (2013) *PLoS One* **8** e59350
11. Chen *et al.* (2012) Chem.Res.Toxicol. **25** 1893
12. Offord *et al.* (1997) Cancer Lett., **114** 275
13. Yogosawa *et al.* (2012) J.Nat.Prod. **75** 2088
14. Kudugunti *et al.* (2011) Chemico-Biol. Interac. **192** 243
15. Chem *et al.* (2004) J.Radiat.Res. **45** 253

400 Davis Dr. Suite 600 Plymouth Meeting PA 19462 • sales@focusbiomolecules.com • 610-994-1134 • focusbiomolecules.com

FOCUS BIOMOLECULES