Proanthocyanidin and its emerging anti-neoplastic effects: recent insights

Shailendra Kapoor

Received: 1 December 2012 / Accepted: 12 December 2012 / Published online: 22 December 2012
© Springer Science+Business Media Dordrecht 2012

To the Editor:

Hassan et al. have provided interesting data in their recent article (Hassan et al. 2012). Proanthocyanidins exert significant anti-neoplastic effects in many systemic malignancies.

Proanthocyanidins markedly reduce the metastatic ability of prostate malignancies. It also augments intratumoral apoptosis while at the same time inhibiting tumor cell proliferation. Proanthocyanidin administration results in downregulation of androgen receptor expression (Uchino et al. 2010). It also mediates this effect by attenuating the activity of the urokinase plasminogen activator (Neuwirt et al. 2008). It also decreases the DNA-binding activity of NF-kappa B. Oligomeric proanthocyanidin complexes are also highly effective in inhibiting prostate cancer growth. They improve the Bax/Bcl-2 ratio within the tumor. It also accentuates p27 activity at the same time. Phosphorylated p42 levels are also increased secondary to proanthocyanidin exposure.

Similar effects are seen in colorectal malignancies. It mediates this role by attenuating phosphorylation of PKB Ser (473). It also enhances caspase-3 activity within the tumor (Engelbrecht et al. 2007). At the same time, it decreases PI3-kinase activity. It especially decreases the formation of “aberrant crypt foci” (Nomoto et al. 2004). As a result, apoptosis is

markedly augmented within the tumors. Similar effects are seen in pancreatic malignancies. It mediates this role by increasing Bax levels while at the same time decreasing Bcl-2 levels (Prasad et al. 2012). PI3K levels are attenuated at the same time. Akt phosphorylation is also mitigated. Overall all these changes result in increased apoptosis within the pancreatic tumors.

Proanthocyanidins are also of clinical benefit in mitigating the side effects of other chemotherapeutic agents. For instance, they reduce cisplatin induced nephrotoxicity. They mediate this protective effect by increasing superoxide dismutase activity (Sayed 2009). Renal glutathione content is also increased secondary to proanthocyanidin administration.

It is obvious from the above examples that proanthocyanidins have significant anti-neoplastic effects. Further studies are needed to fully harness these anti-proliferative effects of proanthocyanidins.

References

- Engelbrecht AM, Mattheyse M, Ellis B (2007) Proanthocyanidin from grape seeds inactivates the PI3-kinase/PKB pathway and induces apoptosis in a colon cancer cell line. *Cancer Lett* 258:144–153
- Hassan HA, Al-Rawi MM (2012) Grape seeds proanthocyanidin extract as a hepatic-reno-protective agent against gibberellic acid induced oxidative stress and cellular alterations. *Cytotechnology*. doi:10.1007/s10616-012-9506-6
- Neuwirt H, Arias MC, Pühr M, Hobisch A, Culig Z (2008) Oligomeric proanthocyanidin complexes (OPC) exert anti-

S. Kapoor (✉)
Chicago, IL, USA
e-mail: shailendrakaipoor@yahoo.com

- proliferative and pro-apoptotic effects on prostate cancer cells. *Prostate* 68:1647–1654
- Nomoto H, Iigo M, Hamada H, Kojima S, Tsuda H (2004) Chemoprevention of colorectal cancer by grape seed proanthocyanidin is accompanied by a decrease in proliferation and increase in apoptosis. *Nutr Cancer* 49:81–88
- Prasad R, Vaid M, Katiyar SK (2012) Grape proanthocyanidin inhibit pancreatic cancer cell growth in vitro and in vivo through induction of apoptosis and by targeting the PI3K/Akt pathway. *PLoS One* 7:e43064
- Sayed AA (2009) Proanthocyanidin protects against cisplatin-induced nephrotoxicity. *Phytother Res* 23:1738–1741
- Uchino R, Madhyastha R, Madhyastha H (2010) NF kappa B-dependent regulation of urokinase plasminogen activator by proanthocyanidin-rich grape seed extract: effect on invasion by prostate cancer cells. *Blood Coagul Fibrinolysis* 21:528–533