

Plant Anticancer Agents and Cancer Chemopreventives: Recent Progress

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There is considerable interest in the screening of higher plant extracts in modern drug discovery programs to discover new chemotypes with potent and selective biological activity.¹ Such work may be performed in different laboratory settings, including those in academic institutions. In the case of cancer, plants offer the potential for the discovery of both cancer chemotherapeutic agents and cancer chemopreventives. To date, the plant kingdom has afforded several structural classes of small-molecule natural products and semi-synthetic anticancer agents that now have clinical use or are in clinical trial.^{1,2} The term “cancer chemoprevention” is relatively modern, and has been defined as “a prevention or delay process of carcinogenesis in humans by the ingestion of dietary or pharmaceutical agents”.³ Several phytochemicals found in dietary plants have been shown to inhibit carcinogenesis in full-term animal experiments. Our recent research directed toward the discovery of plant anticancer agents has been conducted under the auspices of a collaborative National Cooperative Natural Products Drug Discovery Group (NCNPDDG) project.⁴ In turn, our work on cancer chemoprevention is performed as a “program project”, with individual major components on plant collection, phytochemistry, *in vitro* and *in vivo* biology, and synthetic chemistry.⁵ Between these two now well-established natural product drug discovery projects, several hundred plant secondary metabolites representative of considerable structural diversity have been obtained that are active in one or more *in vitro* and/or *in vivo* bioassays, and some of these are under further development through the RAID and RAPID programs of the National Cancer Institute.

The approaches taken and recent progress made in these collaborative multidisciplinary projects to discover new bioactive natural products will be discussed.

Acknowledgment

Funding by current NIH grants U19-CA52956 (A.D. Kinghorn, P.I.) and P01-CA48112 (J.M. Pezzuto, P.I.) (both from the National Cancer Institute, Bethesda, Maryland) is gratefully acknowledged.

References

- (1) Newman, D.J.; Cragg, G.M.; Snader, K.M. *Nat. Prod. Rep.* **2000**, *17*, 215-234.
- (2) Cragg, G.M.; Newman, D.J. *Exp. Opin. Invest. Drugs* **2000**, *9*, 2787-2797.
- (3) Sporn, M.B.; Dunlop, N.M.; Newton, D.L.; Smith, J.M. *Fed. Proc.* **1976**, *35*, 1332-1338.
- (4) Kinghorn, A.D.; Farnsworth, N.R.; Soejarto, D.D.; Cordell, G.A.; Pezzuto, J.M.; Udeani, G.O.; Wall, M.E.; Wani, M.C.; Navarro, H.A.; Kramer, R.A.; Menendez, A.T.; Fairchild, C.T.; Lane, K.E.; Forenza, S.; Vyas, D.M.; Lam, K.S.; Shu, Y.-Z. *Pure Appl. Chem.* **1999**, *71*, 1611-1618.
- (5) Kinghorn, A.D., Su, B.-N.; Lee, D.; Gu, J.-Q.; Pezzuto, J.M. *Curr. Org. Chem.* **2003**, *7*, 213-226.