

Title Screening for cancer chemopreventive agents from cranberry fruit
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Abstract

Diets rich in fruits, vegetables and grains are known to reduce cancer risk in humans. Identification of specific phytochemicals that provide chemopreventive benefits and understanding their mechanism of action will provide opportunities to use diet to promote health. The objectives: 1. Screen cranberry isolates for potential cancer chemopreventive activity using an in vitro bioassay. 2. Use this bioassay to direct the isolation of the active agent(s). Separate extractions of dried cranberry fruit with ethyl acetate, ethanol and water yielded crude solvent extracts. A bioassay based on Murine hepatoma cells (Hepa 1c1c7 cells) was employed to test isolates for their ability to induce quinone reductase (QR). QR is a phase II detoxification enzyme capable of transforming (pro) carcinogens into inactive adducts, representing one tissue defense system to carcinogens. This bioassay was used to direct the isolation of QR-inducing active agents. QR-inducing activity was found only in crude ethanol extracts but not in crude ethyl acetate or aqueous extracts. The level of QR-inducing activity observed in crude ethanol extracts from cranberry fruit was similar to that recorded for broccoli extracts (16,000 inducing units/gdw) in a seminal study in 1992 (Johns Hopkins group) that led to the identification of sulforaphane as a cancer chemopreventive agent. Sephadex LH-20 chromatography using a step gradient up to 100% methanol yielded 5-6 fractions. The three most active fractions contained anthocyanin derivatives. One active fraction was further resolved by preparative reverse-phase HPLC. One purified component shown to be capable of inducing QR was shown to be a cyaniding glycoside based on absorbance spectrum and mass spectrometric analysis. Other and perhaps more potent QR-inducing agents remain to be isolated and identified. Identification of components in cranberry capable of conferring protection from cancer will lead to both health-promoting and value-addition opportunities derived from cranberry resources.