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REVIEW

Emerging therapeutic potential of graviola and its constituents in cancers

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Abstract

Cancer remains a leading cause of death in the USA and around the world. Although the current synthetic inhibitors used in targeted therapies have improved patient prognosis, toxicity and development of resistance to these agents remain a challenge. Plant-derived natural products and their derivatives have historically been used to treat various diseases, including cancer. Several leading chemotherapeutic agents are directly or indirectly based on botanical natural products. Beyond these important drugs, however, a number of crude herbal or botanical preparations have also shown promising utility for cancer and other disorders. One such natural resource is derived from certain plants of the family Annonaceae, which are widely distributed in tropical and subtropical regions. Among the best known of these is *Annona muricata,* also known as soursop, graviola or guanabana. Extracts from the fruit, bark, seeds, roots and leaves of graviola, along with several other Annonaceous species, have been extensively investigated for anticancer, anti-inflammatory and antioxidant properties. Phytochemical studies have identified the acetogenins, a class of bioactive polyketide-derived constituents, from the extracts of Annonaceous species, and dozens of these compounds are present in different parts of graviola. This review summarizes current literature on the therapeutic potential and molecular mechanism of these constituents from *A.muricata* against cancer and many non-malignant diseases. Based on available data, there is good evidence that these long-used plants could have both chemopreventive and therapeutic potential. Appropriate attention to safety studies will be important to assess their effectiveness on various diseases caused or promoted by inflammation.

Introduction

Cancer remains one of the most grave health threats and the leading cause of death in the USA and around the world. The International Agency for Research on Cancer (IARC) reported 14.1 and 8.2 million new cancer cases and deaths, respectively, worldwide in 2012, and are expecting 21.7 and 13 million new cancer cases and deaths, respectively, in 2030 (1). In the USA alone, 1735350 new cases are expected, with 609640 deaths in 2018 (2). Although prognosis of patients with early tumors has significantly improved, limited efficacy and associated toxicity of existing therapies have resulted in significant co-morbidities in patients with advanced tumors. Although these limitations have prompted development of synthetic compounds for molecular targeted therapies, development of resistance to these therapies has also limited their utility (3). Over the past several decades,

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