



Review



Natural products as chemo-radiation therapy sensitizers in cancers

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ABSTRACT

Cancer is a devastating disease and is the second leading cause of death worldwide. Surgery, chemotherapy (CT), and/or radiation therapy (RT) are the treatment of choice for most advanced tumors. Unfortunately, treatment failure due to intrinsic and acquired resistance to the current CT and RT is a significant challenge associated with poor patient prognosis. There is an urgent need to develop and identify agents that can sensitize tumor cells to chemo-radiation therapy (CRT) with minimal cytotoxicity to the healthy tissues. While many recent studies have identified the underlying molecular mechanisms and therapeutic targets for CRT failure, using small molecule inhibitors to chemo/radio sensitize tumors is associated with high toxicity and increased morbidity. Natural products have long been used as chemopreventive agents in many cancers. Combining many of these compounds with the standard chemotherapeutic agents or with RT has shown synergistic effects on cancer cell death and overall improvement in patient survival. Based on the available data, there is strong evidence that natural products have a robust therapeutic potential along with CRT and their well-known chemopreventive effects in many solid tumors. This review article reports updated literature on different natural products used as CT or RT sensitizers in many solid tumors. This is the first review discussing CT and RT sensitizers together in cancer.

1. Introduction

Cancer is a devastating disease and the 2nd cause of death worldwide. International Agency for Research on Cancer (IARC) expects 21.7 and 13 million incidences and deaths, respectively, in 2030 worldwide [1]. While surgery and chemotherapy (CT) and/or radiotherapy (RT) are the standard of care for most advanced tumors, intrinsic or acquired resistance to the CT or RT limits the efficacy and results in poor patient prognosis. Unsurprisingly, 80–90% of cancer-associated deaths are attributed to drug resistance and the development of refractory tumors

[2]. Though the underlying mechanisms of resistance can be multifactorial and completely unknown, recent molecular studies suggest the involvement of deregulated drug targets, pro-survival and anti-apoptotic signaling pathways [3]. In addition, most current chemotherapeutic drugs are toxic to the normal tissues, including the gastrointestinal (GI) tract, heart, bone marrow, lungs, kidneys, etc. [4]. Most importantly, organ failure due to these cytotoxic drugs is a frequent cause of cancer-related deaths [4]. These limitations of the chemotherapeutic drugs have prompted researchers to develop small molecular inhibitors for targeted therapies, but unfortunately, their

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