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Review

Anticancer and Antiviral Properties of Cardiac Glycosides: A Review to Explore the Mechanism of Actions

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Academic Editors: Steve Peigneur and Margherita Brindisi
Received: 29 June 2020; Accepted: 5 August 2020; Published: 7 August 2020

Abstract: Cardiac glycosides (CGs) have a long history of treating cardiac diseases. However, recent reports have suggested that CGs also possess anticancer and antiviral activities. The primary mechanism of action of these anticancer agents is by suppressing the Na^+/k^+-ATPase by decreasing the intracellular K^+ and increasing the Na^+ and Ca^{2+}. Additionally, CGs were known to act as inhibitors of IL8 production, DNA topoisomerase I and II, anoikis prevention and suppression of several target genes responsible for the inhibition of cancer cell proliferation. Moreover, CGs were reported to be effective against several DNA and RNA viral species such as influenza, human cytomegalovirus, herpes simplex virus, coronavirus, tick-borne encephalitis (TBE) virus and Ebola virus. CGs were reported to suppress the HIV-1 gene expression, viral protein translation and alters viral pre-mRNA splicing to inhibit the viral replication. To date, four CGs (Anvirzel, UNBS1450, PBI05204 and digoxin) were in clinical trials for their anticancer activity. This review encapsulates the current knowledge about CGs as anticancer and antiviral drugs in isolation and in combination with some other drugs to enhance their efficiency. Further studies of this class of biomolecules are necessary to determine their possible inhibitory role in cancer and viral diseases.

Keywords: cardiac glycosides; anticancer; antiviral; viral protein translation; signaling pathway; autophagy; preclinical trials; biomolecules

1. Introduction

Global development of cancer registries has led to the discovery of novel drugs that have been derived from natural sources that are used to treat several maladies including cancers and many viral diseases [1]. Several cancers including, breast, lung, liver, colon, gastric, glioblastoma, acute myeloid leukemia and pancreatic cancers pose a constant threat to human health due to the lack of effective therapeutic options, and this incidence is expected to rise by 70% in the next two decades [2]. In addition to these, several viral infections including both DNA (Cytomegalovirus (CMV), herpes simplex virus and Adenovirus) and RNA (chikungunya virus, coronavirus, respiratory syncytial virus, Ebola virus, influenza virus and human immunodeficiency virus (HIV) have also threatened world health due