Chapter 2
Past, Present, and Future of Alkaloid–Based Anticancer Agents

W. H. P. A. D. Perera
Institute of Chemistry Ceylon, Sri Lanka

Mithuni N. Senadeera
Institute of Chemistry Ceylon, Sri Lanka

Dinusha N. Udukala
Institute of Chemistry Ceylon, Sri Lanka

ABSTRACT

Alkaloids are defined as a group of naturally occurring compounds that contain at least one nitrogen atom in their heterocyclic ring. They are abundant in nature, and are a source of pharmacologically significant compounds. This chapter provides an overview of the past, present, and future of the anticancer activity of these secondary metabolites. Based on their chemical structure, biological activity, and pathways of biosynthesis, they can be classified into different classes and are investigated for their anticancer properties. The action of alkaloids depends on how they target the cancer cells, their interactions with cellular components, their impact on cell cycle regulation, apoptosis induction, and angiogenesis inhibition. Numerous scientific advancements have been achieved over the years to enhance their efficacy and reduce their resistance to these alkaloids. Although these naturally occurring compounds have contributed remarkably to cancer treatment, there are challenges and limitations present. Hence, future perspectives of alkaloids are being investigated.

INTRODUCTION

Cancer is a formidable disease characterized by the uncontrollable growth and spread of abnormal cells. A cell undergoes a complex mechanism whereby its genetic material undergoes alterations, leading to the development of a mass of neoplastic cells during the progressive and dynamic process of cancer growth. Cancer development consists of three main interconnected stages: initiation, promotion, and progression. During these stages, the development of the cancer can be interrupted using pharmacologically active ingredients by blocking or suppressing specific molecular events and signaling pathways associated with the spreading of cancer cells (Rather & Bhagat, 2018).

Cancer is one of the major causes of death worldwide, and it is also one of the main barriers to increasing life expectancy in all countries (H. Sung et al., 2021). Therefore, the quest for effective anticancer drugs has become paramount in combating this widespread health challenge.

Alkaloids are a group of secondary metabolites that exhibit a wide array of structural diversity and biological activities. They have been extensively researched for their ability to inhibit cancer cell proliferation and metastasis. Some of the alkaloids that have been isolated from plants have shown notable anticancer activity, both *in vivo* and *in vitro* (Isah, 2016; Lu et al., 2012). Alkaloids are classified based on their biosynthesis, precursor molecules, or based on their structure. Alkaloids can be modified into anticancer drugs with enhanced efficiency, solubility, and stability with the aid of studies on structure-activity relations, hemi synthesis of congeners, and total synthesis (Isah, 2016).

Over the subsequent decades, alkaloids from various plant sources were investigated for their cytotoxic potential against cancer cells. Alkaloids such as Sanguinarine and matrine were identified as potential candidates in early studies. These findings have ignited interest in the therapeutic potential of alkaloids, shaping the trajectory of anti-cancer research.

Modern cancer research has been revolutionized by the isolation and structure elucidation of alkaloids. It has established new principles for the process of developing other new bioactive compounds from natural sources and improved the lives of people.

The future of cancer therapy seems promising as ongoing investigations continue to unveil new insights into the mechanisms of action of alkaloids. Furthermore, the exploration of alkaloids from diverse sources, such as trees and marine organisms, suggests a rich reservoir of untapped potential (Tohme et al., 2011). Alkaloids derived from plants have exhibited significant anticancer properties, opening up new avenues for the development of novel drugs with reduced side effects.

In this comprehensive chapter, we will delve into various classes of alkaloids renowned for their anticancer properties. Our exploration will encompass the mechanisms through which these alkaloids exert their anti-cancer effects, shedding light on their clinical significance. Moreover, we will embark on a journey through the past, present, and future of alkaloids as anticancer agents, providing a holistic view of the evolution and advancements in this field.

This discussion will not only elucidate the historical applications of alkaloids in cancer treatment but will also encompass the current state of research and clinical practices. By examining the mechanisms of action underlying the anticancer properties of alkaloids, we aim to offer a nuanced understanding of their therapeutic potential.

Additionally, our exploration will extend to recent breakthroughs and innovations, reflecting the dynamic nature of alkaloid-based anticancer research. Through this multidimensional approach, we seek to provide readers with a comprehensive overview that bridges the historical foundations, current applications, and future prospects of alkaloids in the realm of cancer treatment effects and enhanced efficacy.

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