Chapter 8
The Role of Terpenes in Cancer Management: Insights From Clinical and Preclinical Studies

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ABSTRACT

Terpenes are a broad and varied group of organic compounds found in numerous plants, especially conifers, and some insects. They are known for imparting aromatic properties to these organisms. Recently, there is a growing interest in terpenes due to their wide-range of applications and increase in demand for natural products. This surge in interest is particularly evident in the cosmetic, pharmaceutical, and food industries, where the demand for natural and organic ingredients has significantly boosted the appeal of terpenes. Additionally, their role in traditional medicine provided a historical context that supported their modern use, and their subsequent role in cancer therapeutics. For the past few decades, numerous studies have been conducted to delve deeper into the potential oncotherapeutic effect of terpenes, with in-vivo and in-vitro studies being carried out rapidly. However, with the lack of clinical trials, the use of terpenes practically as well as commercially, has become questionable in the recent times.

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INTRODUCTION

The origin of the term "terpene" is rooted in the word "turpentine," a fluid commonly obtained from the resin of living trees, especially pines. Structurally, Terpenes are built from isoprene units (C_5H_8) and are classified based on the number of these units into categories such as monoterpenes, diterpenes, triterpenes and sesquiterpenes. Terpenes are hence produced through the mevalonate pathway and the methylerythritol phosphate pathway, both of which synthesize isoprene units that combine to form the various terpenes found today (Huang et al., 2021) naturally sourced from a wide range of plants, including citrus fruits, eucalyptus, tea tree, and cannabis, among others. The history of terpenes is a rich and evolving narrative that spans centuries, reflecting a spectrum from early discovery to scientific exploration. Driven by the demand for consistent and high-quality aromatic compounds for use in fragrances and flavours, the synthetic production of terpenes came into effect in the late 19th century. To add to it, the early discovery of medicinal properties of terpenes dates back to traditional medicine, where plant extracts rich in terpenes were used to treat a variety of ailments. At the same time, the scientific isolation and study of terpenes began in the 19th century to have a basic understanding of the properties and potential therapeutic applications of terpenes with a focus on their chemical structures and biological activities. The first significant use of terpenes in modern medicine was driven by their anti-cancer properties. Taxol, a diterpene derived from the Pacific yew tree, was discovered in the 1960s and developed as a chemotherapy drug, marking a major milestone in cancer treatment. The lasting impact of terpenes is evident in their widespread use across various industries and their ongoing study for potential new applications. Recent research works also highlight the broad spectrum of biological activities exhibited by Terpenes. They include anti-inflammatory, anti-microbial, and anti-oxidant properties. For example, Terpenes like α-pinene, d-limonene, and β-caryophyllene have demonstrated potential in reducing oxidative stress and modulating inflammatory responses (Dash et al., 2022). This diverse functionality makes Terpenes promising candidates for a variety of medical applications.

STRUCTURAL DIVERSITY OF TERPENES

Biologically, terpenes are considered to be the largest class of secondary metabolites derived from plants, and are hence phytochemicals in nature (Ninkuu et al., 2021a). These constitute of isoprene units, thus making them organic compounds