Chapter 15
Advancing Terpenes Through Nanotechnology

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ABSTRACT

Terpenes are among the wide reaching and diversified collection of naturally occurring molecules. Terpenes possess broad range of therapeutic benefits. The ability of terpenes to terminate tumor growth and as a source to prompt cell apoptosis has focused over the anticancer activity of terpenes. Although terpenes act as a potential anticancer agent, nevertheless limited bioavailability is one of the main hitches that restricts the in vivo effectiveness of terpenes. In addition, some terpenes exert toxicological effects that need to confront. In this regard nanotechnology has proven to be an effective approach to pull out the bioavailability barriers with reduced toxicity by means of specific drug activity, enhanced drug permeability and high drug loading efficiency. This review addressed the potential therapeutic benefits of terpenes as anti-cancer agents, as well as the challenges that certain terpenes

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encountered and how nanotechnology can help to overcome them.

TERPENES AND NANOTECHNOLOGY: TARGET DRUG DELIVERY

Terpenes account for the largest class of natural products. These are also called isoprenoids or terpenoids (Chang et al., 2010). Terpenes are made up of several structural isoprene units. Based mostly on the number of isoprene units, they have been divided as sesquiterpene (C15), tetraterpene (C40), monoterpene (C10), diterpene (C20), triterpene (C30), and polyterpene (C > 40) (Liao, Hemmerlin, Bach, & Chye, 2016). Many different plant-based terpenes may have medicinal properties, additionally, a wide range of fascinating terpenoid chemicals with unique structural characteristics are created by marine animals (Yu & Chen et al., 2022; Kim & Li, 2012). Research has demonstrated that terpenes can cause apoptosis in animal models, prevent cell division, and reduce tumor growth (Salehi et al., 2019). Terpenes have direct anticancer effects and improve the effectiveness of traditional chemotherapy in preclinical animals (Park et al., 2011). A growing body of research indicates that terpenes work through a variety of molecular mechanisms to produce their effects. These mechanisms include apoptosis regulation, autophagy induction, blocking cellular signaling pathways, gene expression modulation, angiogenesis inhibition, and inflammation modulation (Magalhaes et al., 2018; Wang et al., 2023).

CONSTRAINTS OF TERPENE USE AS AN ANTICANCER AGENT

Besides being a potential anticancer agent, there are certain limitations associated with the terpenes which are as follows:

Limited bioavailability of terpenes is one of the main drawbacks, which may restrict their effectiveness *in vivo*. Terpenes are extremely hydrophobic compounds that are difficult for the body to absorb and distribute. They are also poorly soluble in water (Luczka et al., 2023; Kamran et al., 2022). Examples include linalool, geraniol, thymol, dl-citronellol, carvacrol, and eugenol (Monia et al., 2017).

It has been reported that some terpenes like limonene, paclitaxel, and nerolidol undergo first-pass hepatic metabolism, reducing the active medication concentration once it enters the systemic circulation. thereby making limited bioavailability a factor (Vieira et al., 2018; Veltkemp et al., 2006; Parvez & Mudavath et al., 2022).