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Review

Phytochemicals intended for anticancer effects at preclinical levels to clinical practice: Assessment of formulations at nanoscale for non-small cell lung cancer (NSCLC) therapy

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ABSTRACT

Over the past few decades, many of the phytochemicals have been shown to possess extraordinary anticancer effects, clinical tested, approved as drugs, and currently in use. A considerable number of phytochemicals either as a single-agent or combined with existing anticancer drugs at pre-clinical and clinical levels have been evaluated to date. However, the clinical trials on phytochemical evaluations against the world's top-ranked cancer, NSCLC, was found to be a very little. Some of the phytochemicals that showed significant anticancer activity against NSCLC *in vitro* and/or *in vivo* at the preclinical levels are highlighted in this review article. There are several impediments such as poor solubility, poor bioavailability, low stability, a requirement of high doses, safety and toxicity that limits the wide-spread use of phytochemicals in clinical oncology. Nanotherapeutic systems can help to overcome the aforementioned issues and wide open the gates to focus on phyto-oncotherapy, in particular NSCLC. The current review aims to summarize the importance of phytochemicals as anticancer agents, with a special mention on nano-formulations to treat non-small cell lung cancer (NSCLC).

1. Introduction

Cancer is one of the serious health problems worldwide. According to WHO, cancer is the second leading cause of death globally. In 2018, an estimate of around 18.1 million people around the world was diagnosed with cancer and 9.6 million deaths were associated with cancer. It has been also estimated that the rate will increase by 50 % in 2020. More than 50 % of the affected will be in the low- and middle-income countries (LMICs). By 2040, the global cancer rate will double from the current rate (29–37 %) and two-third of the occurrence will be in the LMICs. The WHO has also identified lung, breast, prostate, colorectal, stomach, liver, cervical, and thyroid cancers as the most common types of cancers. Table 1 illustrates the incidence of these cancers and the related mortality rate in 2018 [1]. Lung and breast cancers were the most frequently diagnosed (11.6 % of all cases), while lung and colorectal cancers rank top with a high mortality rate (18.4 % and 9.2 % of all deaths, respectively). Consumption of tobacco was found as the primary risk factor and accounts for 22 % of all cancer deaths [1,2]. The American Cancer Society has classified lung cancer mainly into two types, namely non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), shown in Fig. 1. The most common type is the former (around 80–85 % of the cases) and further classified as adenocarcinoma, squamous cell carcinoma, and large cell carcinoma based on the cells from which cancer had originated [3]. Various factors including difficulty in the diagnosis, tumor- and patient-specific heterogeneity of the tumor microenvironment, genomic architecture, genetic and epigenetic

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