



Nanomedicine in Cancer Therapy: Recent Advances and Perspectives

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Nanomedicine has emerged as a major field of academic research with direct impact on human health [1]. Rapid growth in nanotechnology towards the improvement of nanomedicine products commits great prospect to develop therapeutic strategies against cancer. Nanomedicine products represent an opportunity to get advanced targeting strategies and multi-functionality [2]. Nanomedicine assists in maintaining a balance between efficacy and toxicity by specifically accumulating in tumors [3]. The advances in nanotechnology as well as cancer biology have enhanced improvement of drug delivery systems for cancer management with enhanced efficacy and limited side effects. Among them, a variety of nanomaterials based on natural/synthetic polymers, liposomes, metal-organic frameworks (MOFs), gold nanoparticles (NPs) and silica NPs have been used to co-deliver cancer agents and other therapeutics with purpose reducing drug side effects [4]. Several therapeutic nanoparticle platforms, such as liposomes, albumin NPs and polymeric micelles, have been approved for cancer treatment, and many other nanotechnology-enabled therapeutic procedures are under clinical investigation. Nanotechnology has made important contributions to oncology over the past several decades. Liposomes (for example, liposomal doxorubicin (LD); Doxil and Myocet) were the first class of therapeutic nanoparticles to receive clinical approval for cancer treatment. NP albumin-bound paclitaxel (nab-paclitaxel; Abraxane) was the second class of nanomedicines to be commercialized. Polymeric micelles (for instance, Genexol-PM21 and NK105) and polymeric nanoparticles (for instance, CRLX101, BIND-014 and AZD-2811 Accurin24) are two novel classes of cancer nanotherapeutic agent. Ultimate, disappointing clinical results have been reported for

BIND-014, CRLX101 and NK105, underscoring the requirement to reconsider development strategies, including potential patient choice to identify those most likely to respond to nanotherapeutics. Inorganic nanomaterials (for instance, gold nanoshell25, iron oxide NP26 and hafnium oxide NP27) are also being investigated for use in cancer patients, with the iron oxide NP-based NanoTherm26 already marketed in Europe for glioblastoma [5]. Apart from that, mesoporous silica nanoparticles are used as an effective drug carrier in gastric cancer [6]. Nano drug delivery systems enhance the solubility of paclitaxel and other hydrophobic drugs and are less toxic. A PX albumin-bound NP formulation, Abraxane®, has been first FDA approved for treating metastatic breast cancer in 2005 [7]. So far, paclitaxel nanoformulations have been efficiently utilized in clinical practice for the treatment of ovarian cancer, lung cancer, and breast cancer [8]. Furthermore, there has been a great focus on nanotherapy, where the proof-of-concept of cancer prevention using nanoformulations is in a phase of rapid improvement, and naturally occurring bioactive compounds for chemoprevention and chemotherapy in a variety of cancers. Various nanoformulations have been compared to existing cancer medications; they have been shown to be more solvable, stable, effective, and have a better biodistribution pattern, among other things. However, the formation of efficient targeted formulations that can improve therapeutic outcomes without causing significant tissue harm requires attentive assessments [9]. Recent liposomal delivery of the phytochemicals which β -elemene, dioscin, docetaxel, hydroxycamptothecin, paclitaxel, vinorelbine for lung cancer have been studied, curcumin, docetaxel, paclitaxel, piperine and resveratrol for breast cancer have been studied. Moreover, a

phase I study with 96 nonrandomized participants was carried out to assess the effect of liposomal topotecan intravenous injection for the treatment of advanced solid lung tumors. but the trial is reported to enter phase II by the beginning of the year 2023 (NCT04047251). Moreover, an open-label, phase I study on the use of liposomal irinotecan injection was carried out on 136 participants to study its effects on advanced breast cancer and evaluate its efficacy and safety (NCT04728035). Berberine and galbanic acid loaded liposomes have been investigated colon cancer cell lines. A hyaluronan-modified liposome encapsulating curcumin has demonstrated high affinity and cytotoxicity on the acute myeloid leukemia cell surface. Additionally, a liposomal drug-delivery system of vincristine sulfate exhibited specific liposomal adhesion to CCRF-CEM leukemia cell lines and tumor growth reduction, respectively. Recently, curcumin with metal-based flavonoid complexes of ruthenium (II) combined in liposomes exhibited potential against HeLa cervical carcinoma cell lines. Also, curcumin loaded into liposomes has shown various apoptotic efficacies on BxPC-3 and AsPC-1 pancreatic cancer cell lines. The combined liposomes of doxorubicin and linalool nanoemulsions have increased synergistic antitumor effect on epithelial ovarian cancer [10].

Nevertheless, it is important to point out that most of our current understanding of nanoparticles behaviour in vivo is based on animal data, and its translation to nanoparticle behaviour in humans remains largely unexplored [5].

Using nanotechnology we can effectively design nanoparticles that specifically target the tumor site and show no or relatively negligible adverse effects on the environment. The development of nanomedicine would revolutionize the healthcare industry to tackle major health challenges such as cancer.

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