

<u>Current insights into nanodelivery of natural coumarins for anticancer</u> <u>approaches</u> (Review)

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Introduction: Cancer is among the most leading causes of death worldwide. The number of new cancer cases per year is expected to rise to 23.6 million by 2030. Among clinical approaches that have been employed for cancer treatment, use of chemical drugs, alone or in combination with surgery and radiotherapy, is a routine modality. However, severe side effects and rapid emergence of drug resistance in cancer cells are major problems in chemotherapy that need to be overcome. In recent years, nanopharmaceutics has been emerged as an attractive field to develop and improve efficacy of anti-cancer drugs. On the other hand, increasing interest in the use of natural products for cancer chemotherapy has been observed. In this regard, recent studies have reported that the encapsulation of natural products into different delivery systems enhances their efficacy by increasing bioavailability, reducing side effects and improving target-specific activity.

Methods: Published articles including key words cancer therapy, natural coumarins, sustained drug delivery and nanoparticle were extracted in databases PubMed, Web of Science and Scopus.

Results: Coumarins are a large class of phenolic substances found in plants with a wide range of pharmacological properties. Auraptene (AUR) is the most abundant geranyloxy coumarin found in nature with great anti-cancer effects. However, poor solubility of AUR is the main reason for its low bio-distribution and delivery to targeted sites. To overcome this limitation, AUR has been nano-encapsulated with biodegradable and biocompatible copolymers, consist of polycaprolactone (PCL), polyethylene glycol (PEG) and poly-D, Llactide (PLA), which improved therapeutic indexes of AUR. Galbanic acid (GBA) is an active sesquiterpene coumarin that its anti-cancer activities are also limited due to low solubility. Recently, it has been reported that nanodelivery of GBA with PLA-PEG and solid lipid nanoparticles (SLNs) have increased its hydrophilic property. Curcumin is another valuable natural coumarin with poor solubility and bioavailability that both compromise its clinical application to a great extent. Hence, different types of bio-nanocarriers have been used for effective delivery of this agent to different target sites, such as protein-based nanopolymers (including as albumin, zein and silk),



polysaccharide nanoparticles (including chilosan, alginate and cellulose) and copolymers including PCL and PEG.

Conclusion: As proved by recent reports, use of nanocarriers has greatly improved biocompatibility, biodegradation and delivery of natural coumarins. Nevertheless, further in vivo and clinical studies are required to facilitate safe administration of nanocarriers in cancer patients.

Keywords: Nanodelivery, Anticancer effects, Natural coumarins