Concept of Nanomedicine in Endocrine Hormone Cancer Treatment

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Abstract

Cancer is the deadliest disease that led to the death of millions of people around the world. Endocrine cancer is one of the most common types of cancer and badly affects the endocrine system of the patient. Currently, due to the alarming increase in the endocrine cancer patients, there is a need for nanotechnology like therapeutic options to treat the endocrine cancer. This chapter describes about the steroid-based hormone receptors in the cancer biology and remedies like hormone-based therapy to target the different forms of cancers. However, the nanomedicines could be the ideal strategy to treat the endocrine cancer using different forms of nanoproducts. The chapter also briefs about different types of drugs approved for cure of different types of cancer along with their recent status in the market. There is numerous research available in the field of hormone-based treatment for cancer through use of nanotechnology but still no milestone is established.

Keywords

Cancer · Nanomedicines · Hormone · Endocrine

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M. Rahman et al. (eds.), *Hormone Related Cancer Mechanistic and Nanomedicines*,
https://doi.org/10.1007/978-981-19-5558-7_13

13.1 Introduction

Cancer is one of the humanity's most challenging diseases, and it is increasingly becoming a worldwide health issue. Localized malignancies respond well to surgery and radiation therapy, but only chemotherapy can stop the disease from spreading throughout the body. Nanomedicine has progressed in recent years to become a game-changing tool for the treatment and diagnosis of several types of cancers (Feinberg 2004). Scientists are trying to find ligand-based targeted therapeutic techniques with the aid of the conjugation of different drug therapies with a variety of MAbs (monoclonal antibodies) or the ligands that are selectively bound to antigens and receptors on the surface of the tumour cells (Coulson et al. 2014). Despite the fact that this approach outperforms chemotherapy in preclinical and clinical trials, for instance, problems like limited targeted selectivity and potency must need to be considered.

According to statistics, approximately eight million people across the globe and 5,00,000 people in the United States die each year because of the deadly and dreadful disease called "cancer" (Lozano et al. 2012). The chances of cancer occurrence increase with age, and studies prove that it will affect almost 22 million people by the year 2030. Cancer is a disease produced by the spontaneous and regular fragmentation of aberrant cells inside the body. Tumours can be solid or filled with liquid, and in some situations, they can progress to malignancy. It is crucial to understand that not every tumour is cancerous. In general, abnormal tissue growth defines one of the three conditions: malignant, pre-malignant, or benign. According to biopsies, a benign tumour is not a carcinogenic type, and it will not be able to penetrate neighbouring tissues. If removed, it will not relapse, and it will remain confined to its original location without migrating to nearby tissues (Hakim et al. 2015). Haemangiomas, a benign tumour known as strawberry markings, showed an increase in blood. The premalignant type of tumour requires constant monitoring since it has the capability to mature into proper cancer. The malignant form of tumours develops and spreads quickly, attacking neighbouring cells and tissues by making entry into the bloodstream (Lin and Pollard 2007). This is known as the metastatic cancer and proved to be a devastating disease that puts patients' lives in danger. The basic difference between the tumour and cancer is that the tumour is the uncontrolled growth of cells and cancer is the irregular development in the growth of the cells that can be migrated to other parts of the body and damage the surrounding tissues (Loree et al. 2018). The movement of the cells from the specific place of the body to distant regions of organs is known as metastasis. Tobacco use, radiation, loss of daily physical activities, several infections, and obesities are all known to raise the risk of cancer. Nanomedicines are helpful in cancer due to their superior physicochemical and pharmacokinetic features. Nanoparticles, unlike traditional cancer treatments, have several characteristics that put them on a superior list for oncological applications.

The endocrine system is a type of messenger system in which the internal glands secrete hormones in an organism directly into the blood system of circulation. These hormones provide feedback loops that help in the regulation of the targeted organs

residing at distant sites (Lauretta et al. 2019). The adrenal glands and thyroid gland are the principal glands of the human endocrine system. The hypothalamus is the brain activity control center for all endocrine systems. Endocrine glands produce hormones directly into interstitial spaces, where they are absorbed into the bloodstream, irrespective of the duct so called as ductless glands. The pancreas, adrenal glands, pituitary gland, ovaries, parathyroid gland, testes, hypothalamus, pineal gland, and thyroid gland are the primary glands of the endocrine system (Hiller-Sturmhöfel and Bartke 1998). Neuroendocrine organs include the hypothalamus and pituitary gland. Mineralocorticoids, glucocorticoids, and androgens are the three types of steroid hormones produced by the adrenal cortex. Mineralocorticoids (like aldosterone) produced in the zona glomerulosa assist regulate blood pressure and electrolyte balance. In the zona fasciculata, the glucocorticoids cortisol and cortisone are generated, which aid in metabolic regulation and immune system inhibition (Rosol et al. 2001). Three hormones, namely, calcitonin (peptide hormone), T4 (thyroxine), and T3 (triiodothyronine) are released by the thyroid gland. These three hormones of the thyroid gland control the growth and development in children and plays a role in the synthesis of proteins and basal metabolic rate. Homeostasis of the calcium ions is aided with the help of the calcitonin hormone. Thyroid cancer is a very prevalent form of endocrine cancer type and exists in many forms (Cabanillas et al. 2016). Nanomedicine solves biopharmaceutical issues associated with traditional therapies, such as lack of selectivity, drug water solubility, and multidrug resistance (MDR), which results from the repeated administration of the same drug.

Nanotechnology deals with the deliberate creation of substances for practical use in all sectors of sciences by the cutting edge shape and size of the substances based upon the nano-size range of 1–100 nm (Ehdaie 2007). Multi-modular treatment can be obtained by modifying the surface of these nanoparticles (NPs) with diverse moieties such as ligands. Furthermore, the form of NPs has a significant impact on medication uptake and viability in cells. Because of these unique properties, NPs have attracted huge studies in the field of biomedical sciences as a means of transporting cancer therapies (Misra et al. 2010). Nanotechnology-dependent drug delivery systems have improved pharmacokinetic properties, for example, high volume of distribution, good bioavailability to the cancerous cells, and increased clearance value as a consequence of raised enhanced permeation and retention (EPR) effect (Greish 2010). Furthermore, nanomedicine-based techniques would assess molecular alterations and serve as a vital tool for transferring treatments across the biological domains. Nanoparticles having 5.5 nm hydrodynamic diameter can clear the renal track without causing negative effects (Choi et al. 2010). Nanocarriers are appealing because of the safe administration of medications to prevent non-targeted cells and tissues from major unwanted symptoms. The use of nanoparticles as effective carriers is their ease of modification and regarded as distinguished property of NPs. To reduce unwanted side effect and optimize proper response opposite to malignant cells nanocarriers are effective for such aid. However, precise targets, as well as nanocarriers, must be wisely selected. The cure can deposit the medicine in malignant cells by the leaky vasculature with the aid of increased EPR effect (Greish 2010). Furthermore, it becomes crucial to determine the ability of the nanoparticles

as well as the qualities of medicines to predict their capability to cross the biological membrane, their release, and biocapability to deliver the desired medicine to a specific spot.

13.2 Steroid-Based Hormone Receptors in Cancer Biology

Several types of human cancers are affected by steroid hormones throughout their formation and proliferation. As a result, altering the endocrine milieu is an effective palliative treatment for hormone-dependent cancer patients. Many essential cell regulators are mediated by steroid hormone receptors (SHRs), which are intracellular transcription factors that are dependent on the ligand. SHRs are ligand stimulated transcription factors that include receptors for GR (glucocorticoids), ER (oestrogens), PR (progesterone), AR (androgens), as well as mineralocorticoids (MR) (Ahmad and Kumar 2011). They are distinguished by the similarity of certain modular domains, with the DNA binding domain (DBD) providing the most direct link. Certain portions of the SHR proteins fulfil specific tasks, and these areas might potentially be swapped in themselves to generate molecules that function as a hybrid, allowing SHR to function independently. SHRs appear to have a minimum of four key functional regions: C-terminal, NTD (N-terminal domain), DBD (DNA binding domain), and LBD (ligand-binding domain) (Lavery and McEwan 2005). SHRs have tissue and cell-specific actions, as well as developmental-specific regulation, which cause malignancies that include prostate cancer, breast cancer, lung cancer, ovarian cancer, lymphoma, and leukaemia (Miller and Langdon 1997; Huang et al. 2009). The invention of phenomena of the target site selectivity for the modification of the responses of antagonist and agonist. This must focus on the total pharmacological effects of the signal transduction through SHRs with concurrent competition from internal hormones, which is the central issue for SHR pharmacology research (Ahmad and Kumar 2011). The discovery of the underlying mechanisms that control this activity could lead to the creation of tissue-specific modulators SHR. The therapy by the use of the hormones plays a vital role in the cure of numerous malignancies, resulting in a lower death rate and raised lifespan. The main problem of concern is the time period and levels of therapy by hormones in the development of new steroid-based medicines, which could lead to resistance for the steroid over time. The problem has become a serious therapeutic issue, necessitating the production of new drugs to overcome developed resistance in various types of populations of cancer patients.

13.2.1 Leukaemia and Glucocorticoid

Glucocorticoids have been used to treat inflammatory illnesses for decades, and their therapeutic benefits are mediated by changing the transcriptional process of the glucocorticoid receptors through binding to the glucocorticoid receptors (GR) (Schleimer 1993). For many lymphomas, glucocorticoids are the basic parts

of therapy and leukaemia because of their ability to limit malignant cell development and trigger apoptosis (Ploner et al. 2005). The key component contributing to glucocorticoids' therapeutic effectiveness is their ability to decrease inflammation and cause apoptosis. Apoptosis introduced by the dexamethasone in cells of lymphoma occurs via the intracellular route as per the recent understanding of GR-dependent apoptosis in leukaemia (Rambal et al. 2009). Dexamethasone, a glucocorticoid, induces apoptosis in some cell types while having ineffective or anti-apoptotic in others. Various types of mechanisms, include GR isoform expression patterns and post-translational changes, and hypothesized to describe the specificity for cellular apoptotic effect of glucocorticoid. It has been proven that in malignant lymphoid cells, enhanced levels of stimulated intracellular glucocorticoid receptors and an interval of regular exposure to steroids lead to the participation of a complicated signalling process transmission and invoking a network of regulatory mechanisms (Reichardt and Schütz 1998). These GR-mediated lymphoid cell loss mechanisms are influenced significantly by signalling systems cells which have an active role at the level of the process of post-translation. Death of lymphoid cells occurs due to the different kinase mechanisms when working in sequence with the GR (Distelhorst 2002).

A mutation in the GR gene causes glucocorticoid resistance through altering, GR-cofactor interactions, nuclear translocation, ligand-binding affinity, or GR stability. The increased activity of FKBP51 has been linked with glucocorticoid resistance (Scammell et al. 2001). The kinase functional role of p38 MAPKs, ERK, and JNK has also been associated with glucocorticoid resistance (Pace et al. 2007). Combining glucocorticoids with kinase/phosphatase inhibitors has the potential to modify the activity of GR in a gene-specific, cell-specific, and/or time-dependent behaviour (Ismaili and Garabedian 2004).

Incorporating the kinase inhibitors and glucocorticoids and various other types of therapies that treat the response of inflammation is not simple as it seems due to the phosphatases or kinases with signalling glucocorticoid receptors (Beck et al. 2009). As a consequence, extensive studies done for investigating the role of phosphatases and kinases in signalling controlled by the glucocorticoid might lead to novel treatment targets for glucocorticoid-controlled deleterious effects and the lowering of glucocorticoid resistance. Some investigations imply that mineralocorticoids, at least in some leukaemic cells, are accountable for excessive cell growth, which may have therapeutic implications, specifically in resistance related to the glucocorticoid.

13.2.2 Breast Cancer and Oestrogen

The most common malignancy found in women is breast cancer, due to which several types of threat and defensive factors have been established in the last two decades or more (Al-Hajj et al. 2003). The most crucial hormone for the normal activity of the female reproductive system is estrogens and is required for the differentiation and growth of the epithelium of the healthy and normal breast (Bonney et al. 1983). This ovarian hormone impacts cell division rates and hence

affects breast cancer risk by promoting breast epithelial cell proliferation, which is prone to genetic mistakes during the replication of DNA (Subramani et al. 2017). These types of genetic mistakes can eventually result in a cancerous phenotype. Early menarche and late menopause, both of which result in increased oestrogen build-up in the breast epithelium, are well-known threats for breast cancer. Two forms of genes, BRCA2 and BRCA1, frequent in most of the cancer patients, and discovered as genes linked to breast cancer susceptibility (Ford et al. 1998). Breast cancer risk has also been linked to ER gene polymorphisms, that can hinder the linkage of ER receptors to the action factor DNA or any other proteins which coregulates and directly affects the further ER target gene transcription. According to the American Cancer Society, about 60% of premenopausal breast cancers and 80% of those detected after menopause are ER-positive, demonstrating the expression of ER as a potent indicator of responsiveness to endocrine treatment in patients of breast cancer. Estradiol increases proliferation in MCF-7 cells of breast cancer in human by upregulating c-myc, a gene that controls multiple cell cycle-related signalling pathways (Lee et al. 2015). However, disrupting the ER-a signalling system with a pure anti-estrogen completely limits estrogen's apoptotic effect. The ER-a signalling route has been proved to be important for estrogen-induced tumour regression and death. Raloxifene and tamoxifen which are SERMs (selective eestrogen receptor modulators) have proved to show the reduction in invasive breast cancer in the current recent trials in women (Lee et al. 2008). The use of raloxifene plus tamoxifen for the high risk associated with breast cancer in women has been licensed by the US FDA (United States Food and Drug Administration) (Vogel et al. 2010). Following oestrogen deprivation using anti-estrogens, cell death of apoptotic tumour can be induced by the very little number of estrogens. The advancement of new genomic technologies has resulted in the progression of sophisticated tools for identifying genes which are differently expressed between cancers.

13.2.3 Prostate Cancer and Androgen

In males, the most common form of non-skin type of cancer is prostate cancer, and this cancer is prevailing as the second most reason for the death in the United States of America (Scardino 2003). Cancer related to the prostate gland is uncommon before the age of 40, but the disease's risk rises dramatically with age, and exceeds that of any other cancers (Muir et al. 1991). Prostate cancer is 50–70% more common in African/Americans, i.e., Caucasians. Japanese and Chinese males, as well as probably other Asian groups, have lesser chances of being diagnosed with the prostate cancer across the globe (Paris et al. 1999). Androgen, particularly dihydrotestosterone, is required for normal prostate growth (DHTb) (Traish and Morgentaler 2009). AR regulates all the biological activities of androgens. In prostate cancer, AR and its modulators continue to be relevant. Through signal transduction pathways that involve changed expression/binding of AR coregulators, dysregulation of AR function results in prostate cancer progression (Gioeli 2005). During the beginning of prostate cancer, AR expression is profound and can be

observed in the hormone-refractory tumours and hormone-sensitive tumours throughout their course. The most common endocrine-based treatment for prostate cancer is ablation therapy and controlling the circulating testicular androgens (Sriprasad et al. 2009; Labrie et al. 1983). However, deficiency of androgen causes prostate cancer cells to die, these may evolve tolerance to cell death triggered by androgen ablation. A protein generated specifically in the tissue of the prostate called a PSA (prostate-specific antigen) is a widely and normally used biomarker for diagnosis of prostate cancer (Hernández and Thompson 2004). In normal prostate, the PSA levels are more when compared to the serum and serum PSA levels have been found to rise considerably as prostate cancer progresses. PolyQ (polyglutamine) chain repeated sequence encoded by polymeric CAG repeated sequence in the AF1 region of AR gene. The polyQ chain length is inversely proportional to the AR's transcriptional activity (Giovannucci et al. 1997). Because androgens are required for prostate carcinogenesis, and shorter polyQ repeat lengths are linked to increased AR transcriptional activity, it is hypothesized that there are more chances of threat for prostate cancer in males with shorter repeat lengths. The androgen receptor is found on the X chromosome, and it is constant with an X-linked hereditary component for prostate cancer that a brother's history of the disease is riskier than a father (Nelson and Witte 2002). These surprising findings prompted researchers to investigate whether the polyQ chain length in the AR is linked to the development of prostate cancer.

13.2.4 Ovarian Cancer and Progesterone

Ovarian malignancy is the fifth most commonly found cancer in females, accounting for approximately one out of five of all gynaecologic cancers. When ovarian cancer is diagnosed, it has likely progressed to a metastatic stage in most women, resulting in a high fatality rate (Ho 2003). The worldwide use of reproductive medicines that trigger the release of follicles from the ovaries is one of the primary reasons for raised chances of ovarian cancer (Sueblinvong and Carney 2009). Levels of progesterone are quite excess during pregnancy, and certain studies indicate that continual ovulation in females might prone to ovarian cancer (Scully 1995). Some data show that progesterone suppresses the proliferation of ovarian cancer cells in women. It is indicated that the doses equivalent to the progesterone during pregnancy are very effective similarly to the inducers of apoptosis in cells of ovarian cancer and where this mechanism is blocked by estrogens (Dor et al. 2002). In hospital-based investigation, the chance of ovaries-related malignancy for ever use of HRT was 0.9, and in population-dependent survey was 1.1, with no uniform duration—risk relationship. Longer-term usage of HRT has been linked to an augmented risk of ovarian malignancy (Gambacciani et al. 2003). The amount of PR-A isoform action is drastically lowered in tissues of ovaries with specimens of malignant cancer, whereas PR-B is unchanged, showing that PR-mediated transcriptional regulation of the target genes (Akahira et al. 2002). Progesterone has also been shown to limit the proliferation of ovarian cancer cells, perhaps via changing genes such as p53,

c-myc, bcl-2, and others which are apoptotic in nature (Syed et al. 2002; Bu et al. 1997; Yu et al. 2001). Multiple SHR coregulator expression levels must have a critical function in ovarian cancer tissue sensitivity and response to progesterone.

13.2.5 Multiple Endocrine Neoplasia

Multiple endocrine neoplasia (MEN) is categorized into two types: type 2 and type 1. MEN2-A and MEN2-B are further classified in the MEN type-2 (Marx 2005). There are some new classified types of MEN; but somehow, they are placed under these two types: MEN4 is currently thought to be a variant of MEN1, while another variant of MEN2 is familial medullary thyroid cancer (FMTC). Anterior pituitary tumours, parathyroid tumours, and pancreatic islet cell tumours are all symptoms of MEN1 (Trump et al. 1996). The autosomal dominant mode of inheritance is common for MEN1. When the MEN1 linked primary hyperparathyroidism is compared with the non-MEN1 primary hyperparathyroidism, it is seen that MEN1 linked primary hyperparathyroidism is most prone to develop in younger aged individuals and may affect numerous glands (Thakker et al. 2012). Carcinoid tumours of the lungs, gastrointestinal system, pancreas, and thymus have all been reported in MEN1 patients. One of the most common manifestations of MEN1 is cutaneous symptoms. One-third of MEN1 patients have been diagnosed with subcutaneous lipomas. The MEN1 gene which codes for Menin protein is found on the 11th chromosome and has a vital function in genome stability and transcription regulation (Nord et al. 2010). The MEN1 gene has been connected to the loss of heterozygosity in the genomic area, indicating that it can act as a blocker for tumour growth.

Multiple endocrine neoplasia (MEN2)—type 2 is an autosomal dominant disease which affects roughly one in every 30,000 people (Moline and Eng 2011). There are two types of MEN2: MEN2A and MEN2B. The traditional MEN2A, MEN2A with cutaneous lichen amyloidosis (CLA), MEN2A with familial medullary thyroid tumour, and Hirschsprung's disease (HD) are four clinical variations of MEN2A. MEN2 is defined by the coexistence of a number of malignant and benign endocrine neoplasia with non-endocrine disorders such as pheochromocytoma, parathyroid gland adenomatosis. The RET gene, which is responsible for MEN2, has been localized at 10q11.2. There are 21 exons in total. It is a proto-oncogene for tyrosine kinase receptors. Stimulation of the germline point mutations in the RET gene which encodes for receptor tyrosine kinase caused the MEN2A, MEN2B, and FMTC (Santoro et al. 2002). Both MEN2A and MEN2B have a high penetrance and follow an autosomal dominant inheritance pattern. MEN2 can be commonly treated either by visiting to a clinical geneticist or endocrinologist. Individuals with MTC require molecular genetics and biochemical testing for diagnosis and monitoring of their illness state.

13.3 Rationale of Nanomedicine in Hormone-Based Cancer Therapy

Drug delivery has the advantage of eliminating some of the challenges associated with traditional DDS, such as drug absorption while passing through the membrane of cell, insignificant biodistribution, and low bioavailability, all of which impede optimal therapeutic results (Aftab et al. 2018). Targeted DDS in form of nanomedicines is the ideal strategy in this regard. Since it can maintain the needed tissue drug levels as well as plasma concentration inside the body, all types of hazardous effects on the tissues which are fit and healthy in nature are prevented. These DDS reduce healthcare costs by increasing product longevity, product differentiation, and patient compliance. Targeted medication distribution is one of the most significant characteristics since it reduces undesirable toxicity and side effects in the tissues (Dharap et al. 2005). Small capillaries have a diameter of between 5 and 6 microns. Because the diameter of cancer medications is bigger than that of capillaries, they cannot penetrate effectively unless their particle size is reduced. Because nanoparticles are smaller than microparticles, they can easily pass through capillaries and deliver drugs for successful treatment. Furthermore, when drugs are transported by nanoparticles, their efficiency increases because they are efficiently digested by cells. Greater bioavailability, prolonged circulation, improved tumour disposal, appropriate half-life, and transporting the high concentrations of drug at tumour site are all important aspects of nanomedicines (Saha et al. 2010).

13.4 Recent Development in Nanomedicine-Based Hormone Cancer Therapy

FDA is actively creating regulations for items including nanomedicines by forming a "Nano Task Force" that gives sufficient information on the FDA's process for accepting nanomedicines. So far, we've looked into genetic changes that affect tumour prognosis, as well as several targetable biomarkers and imaging techniques that can aid in efficient cancer therapy. Polymer chemistry has progressed because of recent advancements in protein engineering to create complex nano formulations that meet basic criteria (increased pharmacokinetic (PK), safety and controlled release) while also optimizing the delivery system for improved efficacy (via active targeting) and concurrent surveillance of adverse reactions and toxic effects. During the last five decades, endocrine treatment for metastatic prostate cancer has been the primary line of treatment. However, newer kinds of hormonal therapy have broadened the therapeutic options in recent times. Newer options to estrogens and orchiectomy include inhibitors of androgen production, also referred as "antiandrogens," and LHRH (luteinizing hormone-releasing hormone) analogues, which can be used alone or in combination (Labrie et al. 2005). Many people consider orchiectomy to be the "gold standard" form of endocrine therapy since it causes a rapid drop in serum testosterone, although there are concerns regarding the surgery's psychological effects. The recently available antiandrogen flutamide,

when paired with LHRH analogues or orchiectomy, can prevent the "flare," and may enhance survival time, especially when the illness is less severe (Hellerstedt and Pienta 2002). Because LHRH analogues may elicit an initial increase or "flare" in blood testosterone before it declines to castrate levels, they should not be administered alone to individuals with neurologic issues or substantial discomfort. Tamoxifen inhibits the expression of oestrogen receptors in breast cancer cells. It prevents oestrogen from binding to cancerous cells and instructs them to proliferate and develop. Tamoxifen functions as an oestrogen in other types of tissues, such as the uterus and bones, while having an anti-estrogen effect in breast cells. As a result, it is known as a selective oestrogen receptor modulator (SERM). It should be employed to treat both menopausal and non-menopausal women with breast cancer. Hormone-based treatment of cancer has a range of side effects that vary depending on the kind of hormone therapy and how your body reacts to it. Vaginal dryness, hot flashes, lack of interest in sex, changes in your cycles (if you haven't entered menopause yet), weariness, nausea, and mood swings are all possible symptoms. So, recent studies are in pipeline to develop a formulation with lesser side effects and toxicity.

13.5 Clinical Status

Doxil, the first licensed nanomedicine by the FDA, was introduced in 1995. It's liposomal doxorubicin that is been PEGylated. It was licensed for the therapy of Kaposi's sarcoma, refractory breast cancer, and ovarian cancer, and at the beginning. A list of drugs developed under nanotechnology with their advantages is discussed in Table 13.1.

13.6 Conclusion

The efficacy of nanomedicine-based therapy depends on early cancer identification. Nanomedicines are advantageous because they are highly exposed and specific in imaging cellular tumour, making them excellent candidates as one of the best carriers for giving treatments against cancer with minimum damage to normal tissues. The conventional method of drug delivery has a limitation that a huge release of the drug(s) occurs during the circulation of the blood. Traditional systems are affected by the rapid drug(s) release during circulation of blood, so advancement in the availability of nanomedicines provides more beneficial health results. Nanomedicines which act to little modifications in the biological activities may be able to replace current prescription formulations, despite a variety of limitations and flaws. The synthesis flexibility, biocompatibility, optimum size, and long-term release give incredible applications. Hormone-based cancer therapy is the treatment of choice for many cancers like breast cancer, prostate cancer, endometrial cancer, ovarian cancer, and others. But it offers certain side effects along with some toxicities in the patient body, so these should be noticed while considering cancer

Table 13.1 List of drugs developed using nanoengineered approaches in clinicals

S.No.	Name	Constitution	Type of cancer	Approval status
1	*Immunoevasion*			
	Doxil Onivyde	Liposomal doxorubicin (pegylated) Liposomal irinotecan (pegylated)	HV-related Kaposi sarcoma ovarian cancer, and multiple myeloma Advanced pancreatic cancer	Approved in the US (1995) Approved in the US (2015)
2	*Hemodynamics*			
	Nanoparticle generator	Porous silicon micropartticle with polymeric doxorubicin	Breast cancer lung metastasis	planning of phase I
3.	*Protection from degradation*			
	Atu027 ALN-VSP02 DCR-MYC MRX34	Liposomal small interfering RNA (siRNA) Liposomal siRNA Lipid nanoparticle with Dicer-substrate siRNA Liposomal micro-RNA (miRNA)	Advanced or metastatic pancreatic cancer Solid tumours with liver involvement Advanced solid tumours Advanced cancers	Phase I/II completed (2016) Phase I completed (2011) Phase I/II terminated (2016) Phase I terminated (2016)
4.	*Unique electromagnetic properties*			
	Nano Therm AuroShell	Iron oxied NP Gold nanoshells	Brain tumours Prostate cancer	Approved in Europe (2011) Phase I ongoing
5.	*Combination therapy*			
	Vyxeos	Liposomal cytarabine and daunorubicin	High-risk acute myeloid leukaemia	Approved in the US (2017)
6.	*Unique transport properties (EPR) effect Enhanecd permeability and retention*			
	SMANCS DaunoXome Myocet	Polymer-neocarzinostatin conjugate Liposomal daunorubicin	Liver and renal cancer HIV-associated Kaposi's sarcoma	Approved in Japan (1993) Approved in the US (1996)

treatment. Nanotherapeutics have shifted the clinical therapeutic paradigm of cancer from nonspecific chemotherapy (give the appropriate medicine to the correct disease) to site-specific therapy (deliver the right drug to the right spot at the right time).

Conflict of Interest The authors declare no conflict of interest among themselves.

Acknowledgments The authors acknowledge Department of Pharmaceuticals, Ministry of Chemical and Fertilizers, Govt. of India, for their support. The NIPER-R communication number is NIPER-R/Communication/277.

Disclosures There is no conflict of interest and disclosures associated with the manuscript.

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