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Theranostics Usage of Nano Drug Complexes in Clinical Patientcare

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Authors' contributions

This work was carried out in collaboration among all authors. Authors TN and SURN designed the study of proposed hypothesis and compile the scientific contents. Author NT elaborated study to make it more credible. Whereas, author TN managed the literature searches and citation part of the manuscript. Thus, all authors have read and approved the final manuscript.

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Review Article

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ABSTRACT

The extraordinary expansion in the nanomedicine with the development of new nano drug particles made surprising advancement in diagnosis and treatment. Nano drug complexes have amazing medicinal properties and clinical benefits in health care practice. That allows these to attach, absorb and deliver the nano molecule including RNA, DNA, probes and proteins at desired site in an efficient manner. Certain diagnostic agents are potential

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used to theranostics purpose in nano drug's formulation. Additionally the biotransformation technique used to achieve the desired clinical results and/ or pharmacological benefits. The reproducible synthesis of monodispersed nano drug particles play efficient role in healthcare system. Thus, we aimed this study to review the theranostics usage of nano drug complexes in clinical patientcare. The current scientific information used in nano drug particles; non-invasive imaging techniques; and enhanced permeability and retention are tried to incorporate to enhance the credibility of this review article. The medicinal potential of nano drug complexes can effectively be used with the interventions of modern technologies, image guided drug delivery system, antigen targeted immunotherapy and radio-guided drug distribution for individualized and poly-pharmacy practice.

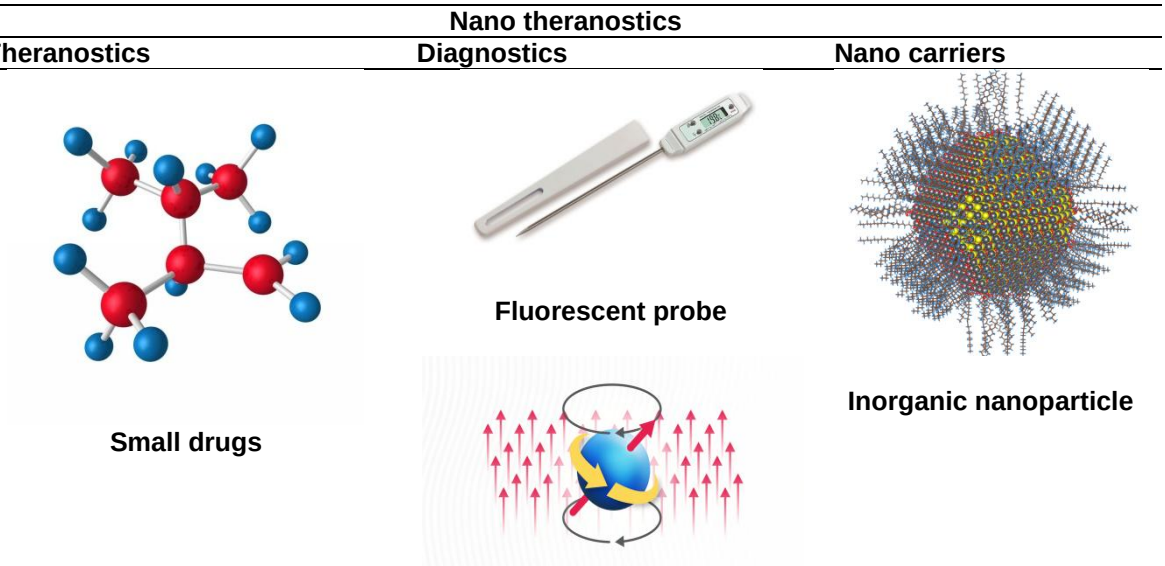
Keywords: Theranostics; nano drug complexes; clinical patientcare; nanoparticles; chemotherapy; targeted drug delivery.

1. INTRODUCTION

The chemotherapy, combination of surgery, radiation therapy and immunotherapy are mostly used for the treatment of critically ill patients. New scientific equipment's and research information has potentially enhanced our ability to design new methods, treatment protocols and understand the pathological complications in microenvironment. The infected cells are composed of vascular, interstitial and non-cellular compartments and predominantly different to the surrounding normal tissue. Therefore, these particular cell compartments have their own cellular characteristics and molecular features. That potentially offered difficulty challenge for scientists to delivery of drugs at desired site within the patient's body [1].

Therefore, we aimed to write this review article with primary information covering the nanoparticles, development of nano carrier, nano drug complexes, drug delivery systems and applications of theranostics. The modern technologies of dendrimers, polymeric nano drug particles, liposomes, nano shells, inorganic nano drugs, metallic micelles and hybrid nano particles are used to improve the accuracy and efficacy of treatment. The magnetic and bacterial nano drug complexes also developed to diversify the drug and with a range of sizes, shapes, and components [2]. That allows the medicinal experts to use the techniques and tools in more efficient manner.

Though, the main objective while designing any drug delivery system is to control drug concentration, that eventually helps to achieve the primary goal therapeutical effectiveness. Additionally, we can maintain a threshold level of drug concentration; reduce cytotoxicity, minimizing the recovery period, improve the patient compliance and allows effective treatment cycles.



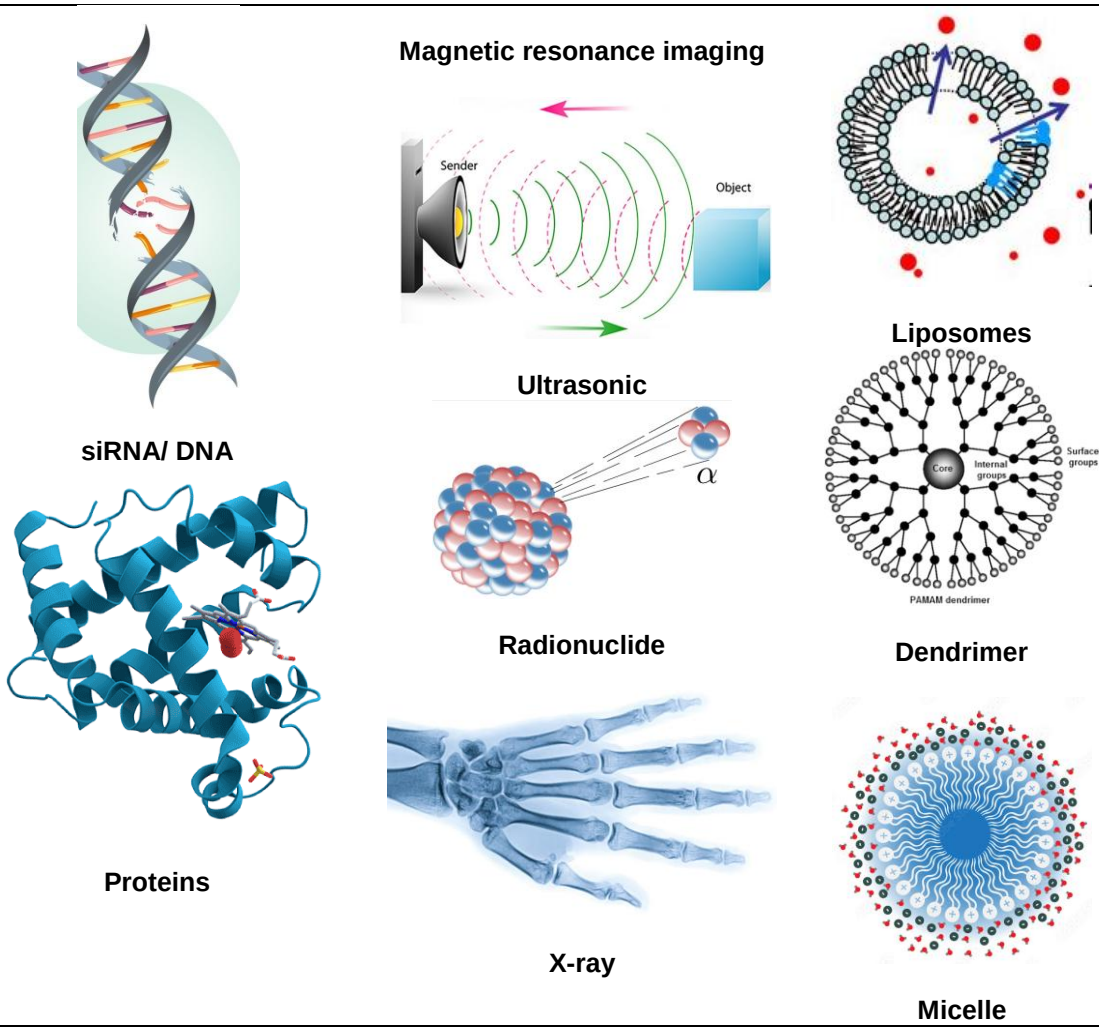
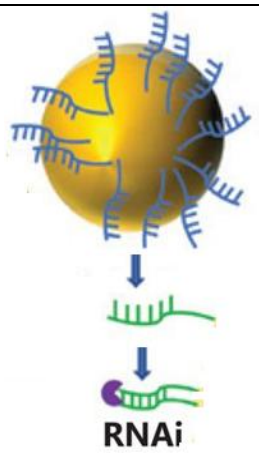
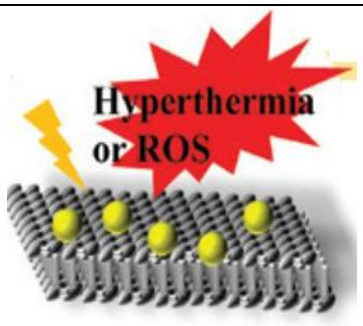


Fig. 1. The theme of the recent developments of nanoscaled theranostic systems for accurate and early diagnosis and effective treatment and/ or management of cancers



Gene Theranostics is the ex-vivo, in-vivo, and in-situ gene therapy along with diagnosis of the severity and stage of



Cocktail Theranostics is the combination of simultaneous administration of multiple therapeutic agents with molecular identification of particular tumor or pathological disorder. It is becoming important for achieving

Chemotheranostics is a combination of drug (chemo-therapeutics agent) and diagnostics. This term describe the usage of anticancer drugs to identify disease and deliver the active drug to

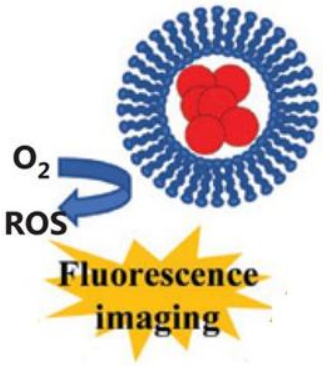
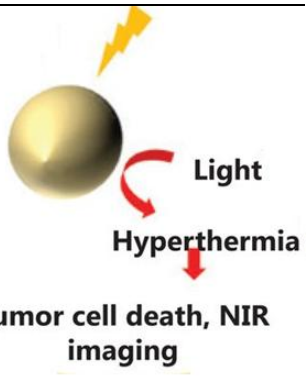
particular disease.	long-term prognosis and control of undesired effects.	treat the main or metastatic tumors.
		
Radio Theranostics is the use of radionuclides for the paired imaging and therapy agents. Radioiodine is the classic radiotheranostic agent that has been used clinically in management of thyroid diseases for nearly 75 years.	**Photodynamic Theranostics** is the usage of photodynamic therapy, activated by light, photosensitizer or photosensitizing agent, to kill cancer cells along with determination of type and stage of disease.	**Photothermal Theranostics** is the utilization of photothermal therapy or physicochemical therapy for cancer treatment (optical radiation in the NIR wavelength range 700–2000 nm) along with application of techniques to identify the disease.

Fig. 2. Nano drug complexes based theranostic systems used for the treatment of different cancers

2. CLINICAL USE AND POTENTIAL CHALLENGES OF NANOTHERANO-STICS

Nanotheranostics is an effective usage of nanotechnology to integrate therapeutic and diagnosis together in clinical practice [3]. That helps the medical professionals to get more accurate information and optimize the clinical outcomes. However, the transformation of nanotheranostic data into understandable clinical information still posed tremendous obstacles in actual medical practice. Therefore, we nanotheranostics system is an outstanding platform to exchange ideas and visions [4].

The scientific community is working to overcome the challenges posed by conventional nanotechnologies including the insufficient drug deposition, uncontrolled cargo release through different smart drug delivery systems and optimization of molecular cell response. However, the controlled delivery system, clinical translation and image guided interventional has introduced considerable obstacle for clinicians to manage certain types of carcinomas. The recent development of nanotheranostics showed viable nanoplatform to provide cancer treatment with various diagnostic techniques [5]. The different kind of magnetic resonance, optical, ultrasonic and computed tomography imaging technologies can potential individualized to design more effective treatment protocols.

However, simultaneous delivery of more than one nano drug complexes at same location has got great attention because of the synergistic drug effects. Development of crosslinked polyion complex micelle of Doxorubicin and Epigallocatechin-3-O-gallate has minimized the cardiotoxicity and resistance [6]. This chemotherapeutic protocol offer synergistic antineoplastic effect along with reduction of associated heart complications. Additionally the early tumor detection is undoubtedly a vital achievement for effective neoplastic therapy. However the correct and precise diagnosis of disease in its early stage remains a difficult challenge. Therefore, an efficient, innovative, cost efficient and quick assay desired to detect a respective genetic components and molecular event that explicitly happened in prostate cancer.

Table 1. Clinical use of nanotechnology to formulate drugs targeting particular entities for the treatment of certain cancers

Cancer type	Therapy	Target entity	Nanoformulation	Active drug
Brain Ca	Photodynamic	Epidermal Growth Factor Receptor	Peptide-targeted gold nanoparticles	Pc 4
Breast Ca	Chemotherapy	Fibrin-associated plasma proteins	CREKA-conjugated liposomes	Doxorubicin
Breast Ca	Chemotherapy	Folate receptors	PLGA polymeric nanoparticles	Doxorubicin
Breast Ca	Chemotherapy	Folate receptors	Deoxycholic acid-O-car-	Paclitaxel
Glioblastoma	Chemotherapy	IL-13Rα2	Liposomes	Doxorubicin
Hepatocellular Ca	Chemotherapy	Integrin receptors	RGD-modified liposomes	Paclitaxel
Epidermoid cyst	Chemotherapy	Epidermal growth factor receptor	PLGA nanoparticles	Tylocrebine
Folate receptor Ca	Photodynamic therapy	Folate receptors	Cobalt ferrite nanoparticles	Hematoporphyrin
Neuroblastoma	Chemotherapy	Transferrin receptors	PEGylated gold nanoparticles	AuNPs
Non-Small Lung Ca	Hyperthermia	Fibrin-associated plasma proteins	CREKA-conjugated dextran- coated iron oxide nanoparticles	Iron oxide NPs
Prostate Ca	Radiotherapy	LHRH receptor	Gold nanorods	Goserelin

[8,9,10,11,12,13,24]

Table 2. Nano-formulations, medicinal component and cancerous cell line

Nanoformulation	Agent	Stimulant	Tested cancer cell lines
Bridged silsesquioxane nanoparticles	Plasmid DNA	Light	Human cervical HeLa cells
Chitosan derivative coated	Doxorubicin	Light/pH	Human cervical HeLa cells
Iron oxide/gold nanoparticles	DNA	AMF	Human cervical HeLa cells
Micelles	Cisplatin + cyanine dye	Light	Cisplatin-resistant lung cancer A549 cells
mPEGylated PLA-conjugated micelles	Curcumin	GSH	Human cervical HeLa cells
PEGylated, RGD-modified, and DSPEIs- functionalized gold nanorods	shRNA	GSH	Human glioblastoma U-87 MG-GFP cells

[14,15,16,17,18,19,20,25]

3. THE NANOPARTICLE DRUG COMPLEX

The nano drug particles used as carriers may attach, entrap or encapsulate to the drug to protect it from destruction, denaturation or degradation. They also offer the simultaneously combination therapy against multiple disorders. The modern technologies can deliver the non-cytotoxic prodrugs i.e. administration of platinum based chemotherapeutic agents [7].

4. KINETIC OF THE NANOPARTICLE DRUG COMPLEX

Nano drug particles are delivered at desired site within patient's body to cure the tumors either passively or actively. The nanoparticles are enabled to exploit the exclusive Enhanced Permeability and Retention effect of tumors in passive delivery [21]. That enables these nano drug complexes to enter into the systemic body circulation or extravascular space, where these active drug agents can gather around the targeted tumor cells. The nano drug complexes particles should be less than 100 nm to obtain best possible pharmacological effect in clinical setting. Distribution of nanoparticles at the particular cancerous cells may not be equal because of the heterogenic blood supply, physiological barriers and interstitial flow and density of the interstitial matrix. However, the active nanoparticles can actively attack to neoplastic cells with the help modification occur at the surface including addition of ligands, peptides synthesis, oligosaccharides, small molecules and antibodies [22]. The nanoparticle can then recognize and attach to the respective complementary target molecules located at the externally exposed or surface structural component of the of cancer cells. The target molecule may be antigen or receptor; therefore it must be in high concentration at the cancer cells but least possible level in the regular normal body tissue. That will potentially help to minimize the toxicity induces by active chemotherapeutical nanoparticles [23,26].

Once the nanoparticle drug complexes delivered to the desired body site to control the tumor, the nano drug complex must dissociate to release the drug into systemic circulation. The drugs particles are then released after binding to neoplastic cells from the respective nano drug complexes. That takes place either by diffusion from the matrix or by erosion, swelling and/ or degradation of the nano drug complexes.

5. CONCLUSION

We have incorporated the most current and authentic information regarding theranostics usage of nano drug complexes in clinical settings. This exclusive attribution may potentially help the clinicians and health care professionals to explore the accurate and rational treatment plans. The potential risks posed during the adjuncts, combination and multiple therapies can be handled more skillfully. However, certain nano drug complexes are translated into new nano drug entities to develop new treatment options. Thus, interdisciplinary collaboration and knowledge exchange between scientists from various disciplines is necessary to make conclusive advancement is this growing field of pharmacotherapy.

6. FUTURE STUDY

We have incorporated the most current and authentic information regarding theranostics and nano drug complexes. Our exclusive attribution may potentially help the scientists to develop advanced pharmacotherapy protocols. However, the researchers are encouraged to develop the novel drugs carriers, therapeutic agents and imaging techniques. The nano drug complexes can be developed to produce the3 ligands, multiple layers with variety of loading density. That will make these agents more suitable for angiogenesis and molecular diagnostics for extravascular targets or theranostics. Nanoparticle formulations designed to reduce excretion, prolong retention and assure the availability at desired pathological site.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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