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A STATE OF THE ART REVIEW ON CANCER NANOMEDICINE

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Abstract

Cancer is known as one of the most daunting health care issues. While there are several approved medications that can be used for cancer therapy, the obstacles to treatment include drug resistance and delivery. In addition, the effectiveness of traditional cancer therapy is often decreased by the pathological features of tumors and their irregular blood vessel architecture and function. It is also important to search for techniques that can improve the therapy's effectiveness, such as nanoparticles (NPs). NPs have many properties, such as their small size, the ability to load different drugs and a wide area of the surface, and the ability to improve conjugate absorption. The NPs were therefore considered as excellent vehicles for tumor-targeting. This study will address the features of various NPs in the treatment of cancer and the advantages of overcoming multidrug resistance. In addition, this study will highlight recent developments in the use of nanomedicine in various cancer treatment techniques, such as chemotherapy, radiotherapy, and immunotherapy.

Keywords: *Clinical, Drug, Medicines, Nanomedicine, Nano.*

I. INTRODUCTION

By either integrating semi-selective properties inherent in nano medicines or by adding complex molecular tags, it is also possible to use nano medicines to improve drug targeting. To date, many nano-medicinal products in clinical development are nano-formulations of medicinal products previously approved that are safer and/or more tolerable than typical systemic delivery[1].

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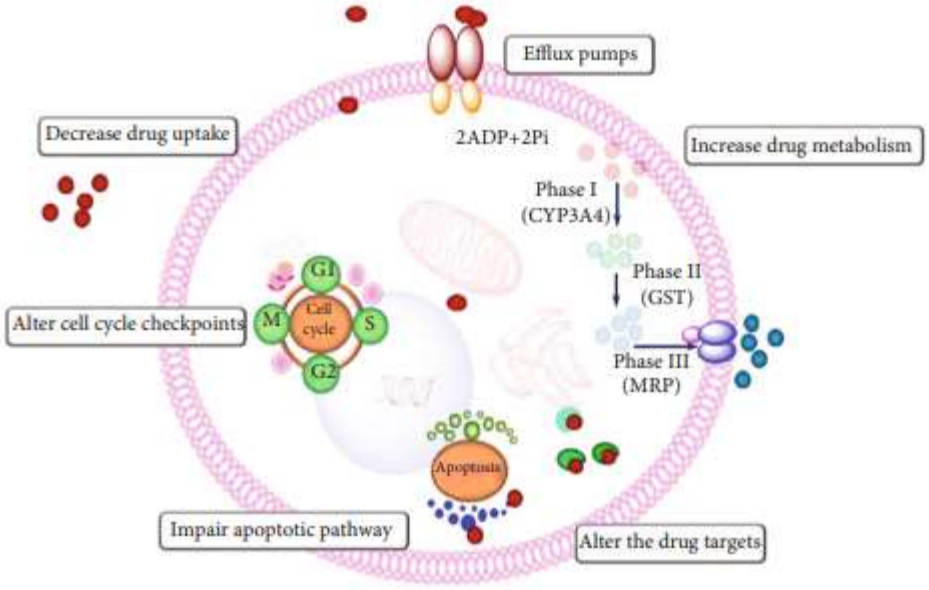

Figure 1: Illustrates the molecular mechanisms of multidrug resistance in cancer[2].

Table 1: Illustrates the Nano formulations of the approved chemotherapies[2].

Name	Chemotherapy	Formulation	Clinical Trial Phase	Investigational Use
MM-302	Doxorubicin	Liposomal	II	MBC
Thermodox	Doxorubicin	Liposomal	III	Hepatobiliary Tumors (with RFA)
CPX-351	Daunorubicin + Cytarabine (7 + 3)	Liposomal	II	High Risk AML
IHL-305	Irinotecan	Liposomal	I	Advanced STMs
MM-398	Irinotecan	Liposomal	III	Metastatic Pancreatic Cancer
Promitil	Mitomycin-C	Liposomal	I	Advanced STMs
Opaxio[1]	Paclitaxel	Polyglumex	II/III	Head and Neck Cancer, GBM, Gyn Malignancies
CRLX-101	Camptothecin	Cyclodextran Conjugated	I/II	Advanced STMs, Rectal Cancer
CRLX-301	Docetaxel	Polymer Conjugated	I (planned)	Refractory Tumors
Genexol-PM[2]	Paclitaxel	Polymeric Micelle	III	MBC, NSCLC
NK-012	SN-38 (Irinotecan Metabolite)	Polymeric Micelle	I/II	Advanced STMs
NK-015	Paclitaxel	Polymeric Micelle	III	MBC
Paclical[1]	Paclitaxel	Polymeric Micelle	III	Gyn Malignancies
SP1049-C[1]	Doxorubicin	Polymeric Micelle	III	Advanced Gastric Cancer
Nanoplatin	Cisplatin	Polymeric Micelle	II/III	Advanced STMs
NC-4016	Oxaliplatin	Polymeric Micelle	I	Advanced STMs
BIND-014	Docetaxel	PSMA Targeted Polymeric Micelle	II	Metastatic Prostate Cancer, NSCLC
DTX-SPL8783	Docetaxel	Dendrimer-Conjugated	I	Advanced Cancer

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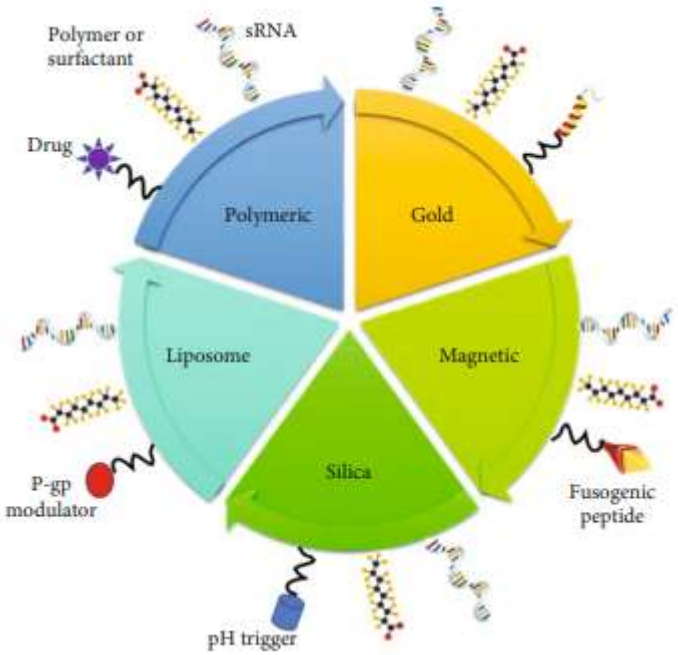

Figure 2: Depicts the mutual drug targeting technology[1].

II. DISCUSSION

Table 2: Illustrates formulated NPs of chemotherapy[3].

Nanoparticle	Medicinal ingredients	Generic name	Cancer type
Liposome NP	Doxorubicin	Doxil	Kaposi sarcoma, ovarian cancer, and multiple myeloma
	Doxorubicin	Myocet	Metastatic breast cancer
	Doxorubicin	MM-302	HER-2-positive breast cancer
	Doxorubicin	Anti-EGR liposome	Many solid cancers
	Doxorubicin	ThermoDox	Hepatocellular carcinoma
	Vincristine sulfate	Marqibo	Acute lymphoblastic leukemia
	Irinotecan	MM-398	Metastatic pancreatic cancer
	Irinotecan	CPX-1	Advanced colorectal cancer
	Paclitaxel	EndoTAG-1	Pancreatic cancer, liver metastases, and HER2-negative breast cancer
	Cisplatin	Lipoplatin	Non-small-cell lung cancer
	siRNA against EPHA2	siRNA-EPHA2-DOPC	Late-stage cancers
	siRNA against PLK1	TKM-080301	Late-stage hepatocellular carcinoma
	MUC1 antigen	Tecemotide	Non-small-cell lung cancer
	HER2 antigen	dHER2+AS15	Breast cancer
	Multicancer-associated antigens	DPX-0907	Ovarian, breast, and prostate cancers
	Melanoma antigens	Lipovaxin-MM	Malignant melanoma
Albumin NP	Paclitaxel	Abraxane	Breast, lung, and pancreatic cancers
Lipid NP	siRNA against PLK1	TKM-080301	Advanced hepatocellular carcinoma
	siRNA against MYC	DCR-MYC	Hepatocellular carcinoma
	siRNA against KSP	ALN-VSP02	Solid tumors
	shRNA against stathmin 1	pbi-shRNA STMN1 LP	Late-stage cancers
Colloid gold NP	TNF, several chemotherapies	CYT-6091 AuNPs	Late-stage cancers
Polymeric micelle	Paclitaxel	Genexol-PM	Breast cancer and non-small-cell lung cancer

By accumulating at higher concentrations in tumours through the Enhanced Permeability and Retention (EPR) effect, nano materials generate outstanding oncologic drug delivery vectors[4]. An abnormally leaky tumour vasculature with reduced lymphatic drainage results in the EPR effect. Nano formulated drugs are substantially larger than free drugs, do not penetrate normal capillaries, and leak out of tumour vessels readily[5]. Recently, the clinical importance of EPR for spontaneous tumours (as opposed to animal models) has become a matter of discussion. With the conjugation of specific molecular tags to the particle surface, the targeting of particles to particular locations can be further improved[6]. Many clinical and preclinical studies have shown that nano-formulated drugs can boost the aggregation of tumours and reduce normal exposure to tissue[7].

Unsurprisingly, nano formulations have been attempted and advanced towards clinical production of several known chemotherapeutics. Many of these, especially Abraxane, have shown clinical superiority over solvent-based formulations and are now widely used in clinical practise. Figure 1 illustrates the molecular mechanisms of multidrug resistance in cancer. Figure 2 depicts the mutual drug targeting technology. Table 1 illustrates the Nano formulations of the approved chemotherapies. Table 2 illustrates formulated NPs of chemotherapy[8].

III. CONCLUSION

Overcoming drug resistance in the treatment of cancer is an important approach and has become more of a concern in recent years. The rapid advancement of the drug delivery system and the progress of nanotechnology give the possibility of creating a more prospective cancer drug resistance strategy. A new strategy for the treatment of cancer therapy could be the creation of NPs. There are, however, some obstacles that should be solved, such as targeting normal cells that share the same cancer cell surface proteins, so selective targeting of cancer cells is not assured. The discovery of a particular surface marker for cancer cells is therefore critical for targeted tumor therapy. This drug prevents highly dividing cells such as cancer cells in the DNA replication machinery. On the other hand, some normal cells, such as epithelial cells of the stomach, break in the acidic environment. This explains the drug's digestive-related side effects. These side effects could therefore be limited by high selective ligands of cancer cells. The problem of nanomedicine also applies to its quality of production. The reproducibility of NPs in large-scale production, particularly the synthesis of homogeneous drug sets, is still difficult.

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