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A Comprehensive Review on Nanomedicine Investigation

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ABSTRACT: ***A relatively new area that is rapidly evolving is nanomedicine. The nanoscale formulation of drugs offers many physical and biological benefits. In turn, these benefits will translate into increased clinical effectiveness and decreased toxicity. Although approximately 50 nano therapeutics have already entered clinical practice, for a variety of indications, a higher number of drugs are undergoing clinical examination. The goal of this analysis is to analyse all of the nano formulations currently undergoing clinical investigation and their ultimate clinical translation outlook. The relatively new field of science is nanomedicine, the application of nanotechnology to health and medicine. While nanotechnology has many applications in medicine, the development of nanoparticle-based therapeutics has been a key application. Physical benefits such as increased solubility, decreased degradation or physiological clearance rates, decreased systemic toxicity, and improved clinical effectiveness are imparted by the introduction of nano materials into the drug formulation (nano formulation). Many of these features are not intrinsic to individual particles due to rapid developments in material sciences, but are under tuneable control, enabling the precise production of drug delivery vehicles with the most desirable physical properties.***

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

INTRODUCTION

It is also possible to use nano medicines to enhance drug targeting by either incorporating semi-selective properties inherent in nano medicines or by adding complex molecular tags. Many nano-medicinal products in clinical development to date are nano-formulations of previously approved medicinal products that are more safe and/or tolerable than conventional systemic delivery[1].

Table 1: Illustrates the Approved Nano therapeutics[2]**.**

Trade Name	Formulation	Indication	Initial Approval Date
Exparel	Pegylated Adenosine Deaminase	SCID[7]	1990
Oncospar	Pegylated Asparaginase	ALL	1994
Doxil	Liposomal Doxorubicin	Kaposi's Sarcoma, Ovarian Cancer, MBC[7]	1995
Abelcet, Amphotec, Ambisome	Liposomal Amphotericin B	Fungal Infections	1995, 1996, 1997
Copaxone	Glutaramer Acetate	Multiple Sclerosis	1996
Ferumoxsil	Siloxane-Coated Iron Oxide	Oral Contrast Agent	1997
PegIntron	Pegylated Interferon α-2b	Hepatitis C	2001
Pegasys	Pegylated Interferon α-2a	Hepatitis B, C	2002
Neulasta	Pegylated Filgastrim	Chemotherapy-induced Neutropenia	2002
Abraxane	Albumin Bound Paclitaxel	Advanced lung, pancreatic, breast cancers	2005
Feraheme	Carbohydrate-Coated Iron Oxide	Anemia of Chronic Kidney Disease	2007
Depocyte	Liposomal Cytarabine	Lymphomtous Meningitis	2007
Exparel	Liposomal Bupivacaine	Post-operative Pain	2011
Sienna+	Dextran-Coated Iron Oxide	Sentinal Lymphnode Mapping[7]	2011
Marquibo	Liposomal Vincrisitine	Adult AML	2012

Table 2: Illustrates the Nano formulations of the approved chemotherapies.

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

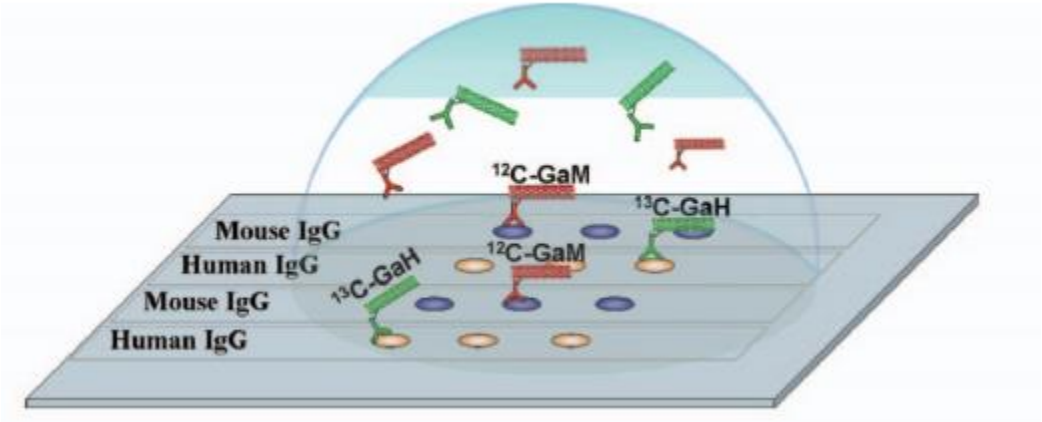

Figure 1: Depicts the schematic diagram of a protein microarray[3]**.**

A number of drug delivery platforms, including protein/polymer-drug conjugates, polymeric micelles, liposomal preparations, dendrimers, and inorganic metal nanoparticles, are used to formulate these drugs. New nano therapeutics are entering clinical trials every year with rapid progress in this field[4]. As the status of clinical translation is essential to the science of nanomedicine and can guide future research directions, we strive to provide an up-to-date overview of all nano therapeutics in research. Table 1 illustrates the Approved Nano therapeutics.

Table 2 illustrates the Nano formulations of the approved chemotherapies. Figure 1 depicts the schematic diagram of a protein microarray[5].

An enticing application of nanoparticle drug delivery is dual drug delivery with co-encapsulation of drugs in particles. Optimal drug ratios and drug dose sequences can be established in vitro, but maintaining these spatial and temporal distribution characteristics in vivo at the cellular level is very difficult. Nanoparticles may be formulated to deliver drugs sequentially within the tumour microenvironment at precise molar ratios.

DISCUSSION

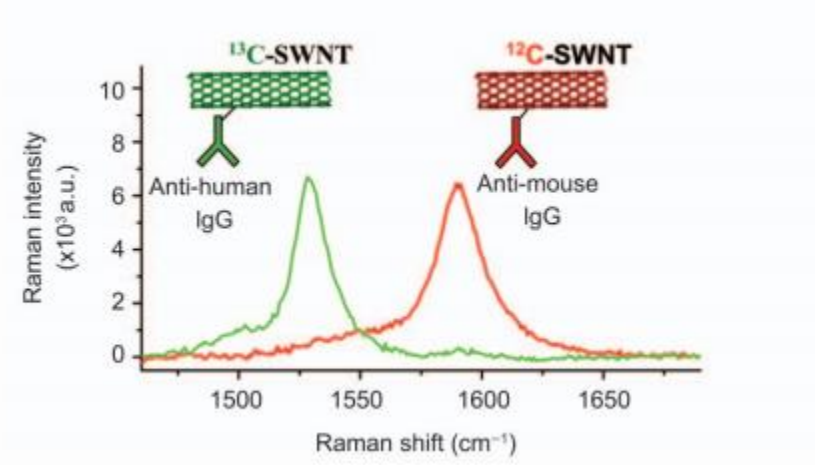

Figure 2: Illustrates the G-band Raman scattering spectra[6]**.**

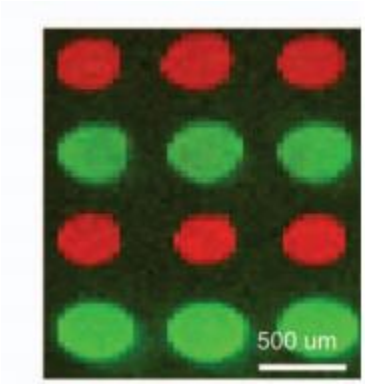

Figure 3: Illustrates the direct Raman detection of mouse[7]**.**

By accumulating at higher concentrations in tumours through the Enhanced Permeability and Retention (EPR) effect, nano materials generate outstanding oncologic drug delivery vectors. An abnormally leaky tumour vasculature with reduced lymphatic drainage results in the EPR effect.4 Nano formulated drugs are substantially larger than free drugs, do not penetrate normal capillaries, and leak out of tumour vessels readily. 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. Many clinical and preclinical studies have shown that nano-formulated drugs can boost the aggregation of tumours and reduce normal exposure to tissue.

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.

CONCLUSION

Nanomedicine, in its short existence, has come a long way. There are a large number of nano medicines, as detailed in this study, that have progressed into clinical trials, many of which display promising results. While regulatory approval is ultimately obtained by only a small number of preclinical systems, the sheer number of current preclinical trials suggests that many new nano-medicines should eventually come onto the market. In addition, the pace of technical developments in nano engineering is rapid, and the number of systems available continues to grow rapidly. While the translation of novel therapeutics still faces many obstacles, developments in nanomedicine have the potential to radically alter the clinical landscape and enhance our therapeutic and diagnostic armamentarium.

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