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NEW ADVANCES IN STRATEGIES OF NANOTECHNOLOGY TO OVERCOME PANCREATIC CANCER

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Abstract: One of the most common types of cancer in developing nations is pancreatic cancer. Up to 90% of pancreatic cancers are caused by pancreatic adenocarcinoma, and pancreatic neuroendocrine tumour, a less prevalent variety that accounts for 5% of all malignancies, are the two main types of malignant tumours of the pancreas. Pancreatic cancer continues to be one of the deadliest illnesses and demands immediate attention owing to its extremely poor overall survival rate, which claims many lives each year throughout the world. Two of the main obstacles in the fight against cancer are early detection and effective treatments. In the current study, we evaluated effective pancreatic cancer treatment methods and in-depth highlighted the most recent advancements in contemporary medication delivery methods that are centered on and generated from nanotechnology. Recent advances in drug delivery systems based on nanotechnology have aimed towards improving cellular absorption, enhance pharmacokinetics, and improve the efficacy of anti-cancer drugs. The current review provides information on recent developments about possible therapeutic targets for the treatment of cancer of the pancreas. This information may serve as a foundation for the future creation of multifunctional nano-constructions for the early diagnosis and effective treatment of pancreatic cancer.

***Keywords*: Pancreatic Cancer, Nanotechnology, Diagnosis, Targeting Therapy, Drug Delivery Systems**

I. INTRODUCTION

Pancreatic cancer stands as one of the most lethal cancer diagnoses globally, exhibiting a remarkably low 5-year survival rate of merely 9.3% across populations worldwide. It is a type of cancer that has pancreatic origins (American Cancer Society, 2017). A particular class of organ in the human body is the pancreas, which comes after the abdomen. It is somewhat similar to the shape of a fish with a variable head, pointed body, and slim, pointy tail. In adults, it is less than 2 inches (5 cm) wide and measures around 6 inches (15 centimeters). When exocrine cells in the pancreas progress out of control the most prevalent kind of pancreatic cancer i.e., pancreatic adenocarcinoma, develops. Endocrine cells make up a smaller percentage of the cells in the pancreas, which also generates vital hormones like insulin and glucagon that serve to regulate and release blood sugar levels into the circulation. The pancreatic tumor develops in the endocrine cells of the pancreas.

1.1 Types of Pancreatic cancer

The most typical kind of pancreatic cancer is exocrine cancer. There are several varieties of exocrine carcinoma.

- Pancreatic Adenocarcinoma.
- Pancreatic neuroendocrine.

1.2 LEVELS OF PANCREATIC CANCER

Different stages of pancreatic cancer are presented below. They are;

- **Stage - 0**; There are abnormal cells, but they haven't spread to the nearby tissue. Patients could develop carcinoma in situ, often known as CIS, which could spread to neighbouring normal tissue.
- **Stage - 1;** At this phase, cancer has developed and its pancreatic roots are known. The tumour is categorized into Stages IA and IB based on its size. Stage IA has a size reduction of 2 cm, whereas Stage IB has a size increase of 2 cm but not more than 4 cm.
- **Stage - 2;** In comparison to the initial stage, the cancer tumour has grown larger and has spread to nearby tissues. This level is divided into Stage IIA and Stage IIB categories. In IIA, the tumour is more than 4 cm, and in IIB, the tumour is of any size, also the cancer cells have spread into 1 to 3 neighbouring lymph nodes**.**
- **Stage - 3;** Four or more adjacent lymph nodes or the main blood vessels close to the pancreas may be affected by cancer. At this point, the tumour can be of any size. This includes the porch vein, greater mesenteric artery, celiac axis, and mutual hepatic artery.
- **Stage – 4;** The metastasis of cancer cells has extended to distant regions throughout the human body. This form of tumour exhibits variable sizes, and its malignant presence has infiltrated vital organs such as the liver, lungs, and peritoneal cavity**.**

1.3 Signs of pancreatic cancer

There may be no early warning signs or symptoms for pancreatic cancer., the major signs of pancreatic cancer are listed below.

- Jaundice (a skin and eye white yellowing condition).
- Light-coloured stools
- Bloody urine
- Back and upper or middle abdominal pain.
- Extreme fatigue
- Loss of weight.
- A decrease in appetite.

1.4 Risk Factors Associated with Pancreatic Cancer

- Several factors are considered as risk factors for pancreatic cancer, some of risk factors are ;
- Smoking
- Overweight
- Personal experience with diabetes or recurring pancreatitis
- Family history of pancreatic cancer
- Some inherited conditions
- Multiple endocrine neoplasia type 1 (MEN1) syndromes
- Hereditary nonpolyposis colon cancer (HNPCC; Lynch syndrome)
- Von Hippel-Lindau syndrome
- Peutz- Jeghers syndrome
- Hereditary breast and ovarian cancer syndrome
- Familial atypical multiple mole melanoma (FAMMM) syndromes
- Ataxia-telangiectasia

1.6 Diagnosis of Pancreatic Cancer

Lab Tests, Imaging Tests and Biopsies are the diagnostic testing procedure, which can detect pancreatic cancer.

1. **Lab Tests**: High or low concentrations of these chemicals (Biomarkers and Harmones) in the human body may signal cancer. Lab tests could also help doctors make diagnoses. On the other hand, abnormal test results may not always be a symptom of cancer.

2. **Imaging Tests**: Imaging tests produce images of several bodily regions that help the doctor to determine whether tumour is present or absent. Types of various Medical Image Scanning are outlined below; Ct Scan, MRI Scan, Nuclear Scan, Pet Scan (Positron Emission Tomography), Ultrasound Scan

3. **Biopsy Test:** In the course of this, the doctor obtains a tissue sample. A pathologist examines the tissue under an optical microscope and does many tests to determine whether the soft tissue is cancerous. The biopsy sample can be collected in many ways and some are shown below:
Needle: A needle is used by the doctor to remove tissue or fluid. This method is used for liver, breast, prostate, and "bone" marrow biopsies.
Endoscopy: The surgeon uses a tiny, lit tube called an endoscope to view areas inside the body through regular body openings like the mouth or anus. If the doctor detects abnormal tissue during the test, they will remove the abnormal tissue with part of the neighbouring normal tissue using an endoscope.

1.7 Treatment of pancreatic cancer

Depending on the severity of the illness, a patient may have surgery, ablation or embolization treatment, radiation therapy, or chemotherapy for pancreatic cancer. Surgery is only one effective medical care option for pancreatic cancer. Even though most of the patients with this cancer are discovered at an advanced stage, only 20% of patients are ready for surgical therapy. Even though the malignancy has been removed, this patient has an average life expectancy of just 1.12 years and a five-year relative survival rate of 10–20 percent.

A) Chemotherapy

Cytotoxic chemotherapy is a popular drug used to treat non-resectable pancreatic cancer. There have been reports of several cytotoxic agents being used in phase 2 and 3 studies worldwide as a single medicine or in combination with other therapies. In a trial, fixed dosages of S-1 (a new xuoropyrimidine derivative drug) and GEM were examined along with the ideal radiation dose in instances of non-resectable pancreatic cancer. For these patients, the median overall survival (OS) and progression-free survival (PFS) were 16.0 and 11.0 months, respectively. In a separate trial, Sherman et al. examined neoadjuvant GEM, docetaxel, and capecitabine in patients with locally advanced unresectable pancreatic adenocarcinoma disease brought on by arterial or severe venous involvement. Patients received GEM, docetaxel, and capecitabine through both venous and arterial arms. All patients' median OS was 32.5 months, compared to 29.0 months for arterial patients and more than 42.0 months for venous patients. Over 34.0 months, the illness was free in three cases. Patients in the venous arm group had a significantly greater survival rate than those in the arterial arm group.

B) Radiation therapy

The most lethal tumours discovered in humans, pancreatic cancer is thought to have a dramatically increased incidence rate during the previous six years. Most patients are diagnosed at an advanced stage when they are first seen, at which point radiation therapy may be more appropriate than surgery. High intensity X-rays are utilised in radiotherapy (RT), which is primarily delivered using linear accelerators. Both healthy and malignant cells are damaged by radiation, but healthy cells are less vulnerable to the treatment's side effects since they have a natural tendency to repair themselves. Radiation therapy is a recognized cancer treatment. The radiation type used to treat pancreatic cancer is an external beam of different radiations that are focused from an external source. This could be administered as adjuvant therapy after surgery to lessen the risk of cancer recurring. Chemoradiation, as it is commonly known, is the application of radiation treatment to cancers

that are just barely amenable to surgery. In certain situations, chemoradiation is administered beforehand as neoadjuvant therapy, which promotes tumour reduction and makes total tumour removal easier.

II. NEW DRUG DELIVERY SYSTEMS FOR THE TREATMENT OF PANCREATIC CANCER

2.1 Liposomal drug-delivery systems for Pancreatic Cancer Treatment

2.1.1 Doxorubicin in pegylated liposomal form, Caelyx/Doxil;

Doxorubicin has been successfully contained by liposomes. In s.c. AsPC-1 pancreatic tumour xenografts, preclinical investigations have shown that Doxorubicin in pegylated liposomal form, which only had minor overall negative consequences and shown increased medication concentrations inside tumours, dramatically increased the therapeutic efficacy. Octreotide modification improved doxorubicin-loaded liposomes' transport to and targeting of the pancreas, where the somatostatin receptors are strongly expressed, according to a newest in- vivo research. In comparison to free doxorubicin or standard liposomal doxorubicin, Doxorubicin in pegylated liposomal form, Caelyx/Doxil exhibits a significantly longer circulation time, a smaller volume of distribution, and a slower rate of plasma clearance. The effectiveness of Caelyx/Doxil in treating AIDS-related Phase I/II investigations in patients with solid tumors, including pancreatic cancer, were conducted as a result of Kaposi's sarcoma. However, in two phase II investigations on pancreatic cancer, no significant responses were seen. In a later phase I trial, Caelyx was combined with mitomycin C, weekly 24-hour in fusional 5-fluorouracil, and folinic acid to treat 12 patients with pancreatic cancer who were unresponsive to gemcitabine. Three of them had tumor shrinking that could be seen. A 6.5-month median survival was recorded.

2.1.2 ONCO-TCS (liposomal vincristine);

There has been little clinical research on vincristine contained in 120 nm tiny unilamellar vesicles made of cholesterol liposomes containing distearoylphosphatidylcholine.Lipid-based vincristine (ONCO-TCS) has a longer half-life than free vincristine, less neurotoxic and accumulates in lymph nodes and tumours rather than brain tissue in both experimental animals and people than free vincristine. Its greater efficacy was attributed to vincristine's higher dosages, changed pharmacokinetics and tumor-specific deposits.

2.2 PDAC metastasis prevention using a nanomedicine approach

PDAC is a very deadly cancer that is becoming more common and more lethal. Due to delayed and vague clinical signs, metastasis—which accounts for a significant portion of PDAC deaths—is present in more than 80% of patients at the time of diagnosis. As a result, one of the main therapy challenges for PDAC has been preventing metastasis. Killing cancer stem cells in the main niche to stop their dissemination into the bloodstream and concentrating on circulating tumour cells to stop the growth of metastatic foci are the traditional aims of anti-metastasis therapy. With improvements in nanomedicine and nanotechnology as well as our understanding of how tumours spread, TME (tumour microenvironment) and exosome involvement in metastasis have been highlighted in recent years. Pancreatic cancer can be prevented by the innovative tactics of TME remodelling and the removal of carcinogenic exosomes by Nano Systems.

2.3 Combination therapy for pancreatic cancer

Albumin-bound paclitaxel (Abraxane® or nab-PTX) has fixed the problems with the paclitaxel medicine by having an acceptable solubility in water. Paclitaxel has been reported to increase the amount of Gemcitabine in tumour cells by lowering the action of cytidine deaminase, an enzyme that can slow down Gemcitabine metabolism.The PanCa cells' stroma can be distorted by nab-PTX, which also helps to activate angiogenesis. This increases circulation, which makes it simpler for GEM to reach the targeted areas. Notwithstanding these benefits, this medicine combination has demonstrated severe toxicity, necessitated effective research and tested before the drug can be approved. Phase I and Phase II clinical trials on GEM and nab-PTX established the highest dose tolerable of GEM and nab-PTX for treating PanCa as well as their response to positron emission scan analysis, which helps identify the stromal changes in the pancreas and affects drug uptake. Successful clinical trials have established a typical combinational dosage of 1000 mg/m2 GEM and 125 mg/m2 nab-PTX administered for a 3-week period in repetition every 4 weeks. These research findings revealed much higher full response rates, overall survival rates, and highest dosages tolerated. As a result of their preclinical study, which showed that nab-PTX is intended to kill the peritumoral desmoplastic stroma, they have increased the

internalization of tumour of GEM within the treatment mice group that they employed for their inquiry. Even though these studies advised on how to utilize it successfully against PanCa, a randomized phase III clinical investigation is necessary to establish this combination drug as an appropriate one for the effective treatment of PDAC.

2.4 Photodynamic therapy for treatment of pancreatic cancer

Laser-triggered photodynamic treatment (PDT), in contrast to traditional chemotherapy, is a different method of tumour ablation, particularly for tumours that are resistant to chemotherapy and radiation. For both benign and malignant tumors, it uses light at a precise wavelength to stimulate nontoxic photosensitizers, which then produce toxic reactive oxygen species (ROS) and destroy tissue and vasculature. Due to its ability to destroy cancer cells via a variety of mechanisms, PDT can be a less intrusive therapeutic strategy. In 2002, 16 patients underwent PDT with intravenous injection of the photosensitizer (PS), meso-tetra hydroxyphenyl chlorin (mTHPC), in the first report on the use of PDT in clinics. Significant tumour necrosis was seen, and the median duration to survival with PDT is 9.5 months (range 3-40). Although more research on PDT use in PDAC is needed to prove the effectiveness of the treatment. The same team recently assessed the second-generation PS, known as verteporfin, in 15 patients with advanced PDAC. The induction of tumour necrosis had less negative effects than in their earlier work.

2.5 Pancreatic cancer therapy with exosomes

Exosomes released by cancer cells of Pancreas and the cells that surround them can interact with one another by attaching to the relevant receptors on the membrane of the cell, which causes tumour variations and heterogeneity in the cells that are involved in the tumour as well as the microenvironment. Exosomes have a key role in promoting carcinogenesis, proliferation, and metastasis, as was previously indicated. They are also engaged in a number of pathological processes and the remodeling of the microenvironment.

2.5.1 Exosomes as therapeutic agents;

Exosomes are essential for the development of treatment resistance and the spread of pancreatic cancer, as was previously mentioned. As a result, the current therapy approach focuses mostly on reducing cancer cell exosome synthesis and preventing receptor cells from absorbing particular exosomes.
Exosome-targeted treatment aims to prevent recipient cells from absorbing exosomes. Exosomes generated from malignancy are internalized by heparan sulphate proteoglycans (HSPGs). Exosome uptake is considerably reduced by enzymatic reduction of cell surface HSPG, which is colocalized with internalized exosomes and HSPGs of the syndecan and glypican types.

2.5.2 Exosomes as nano transporters;

Exosomes may transport different nucleic acids and proteins that recipient cells can absorb. Because of the biological properties of recipient cells, these cells are excellent drug carriers. Exosomes can be used to deliver drugs that are toxic or immunogenic to target cells, preventing systemic toxicity. Paclitaxel (PTX), which may drastically limit the spread of pancreatic cancer cell lines, can be packaged and delivered by MSCs through exosomes. Additionally, Kim et al. verified that the inclusion of exosomes containing PTX may boost cytotoxicity by a factor of more than 50 in drug-resistant cells. The distribution of chemotherapeutic medicines and the treatment of drug-resistant malignancy have significant potential for the PTX-loaded exosomes.

2.6 Gold nanoparticle-based photothermal therapy for pancreatic cancer

Because of its benefits, GNP-based Photo thermal therapy has been developed as a platform for tumour elimination invivo and has undergone successful clinical testing. First off, GNPs are biocompatible and can have medicinal moieties or targeted ligands added to their surfaces. Second, a variety of gold nanostructures can be created, such as nanospheres, nanorods, or nano shells and their effectiveness can be determined in a variety of experimental contexts. GNP's size and shape affect its capacity to both scatter and absorb light. Due to their adjustable optical characteristics and displaced SPRs to the NIR, nanorods and nano shells exhibit higher photothermal effects than nanospheres (650-1350 nm). With little impact on healthy tissues, this

tunability allows laser energy to penetrate deeply into tumour tissues. In order to study the impact of their Iron-oxide core/gold-shell nanoparticles of 30 nm size on Panc-1 cells, Guo et al. Following NIR radiation, the viability of cells treated with iron/gold-shell nanoparticles at concentrations of 0, 25, or 50 μg /mL was 61%, 21.9%, or 2.3%, compared to 100%, 71.3%, and 47.0% for control cells. The authors came to the conclusion that GNPs were an effective photosensitizer for pancreatic cancer photothermal ablation.

2.7 Nano-liposomal formulations

Nano-liposomal formulations are a type of drug delivery system that can increase the effectiveness of chemotherapy drugs while cutting down on their damaging impact on healthy tissues. They achieve this by encapsulating drugs with different chemical properties in tiny liposomes. Gem Elaidate-loaded PEGylated nanoliposomes (PGPLs) have been developed as a potential treatment for pancreatic cancer (PDAC). These nanoliposomes have a higher drug loading and positive surface charge, which may enhance their anti-cancer activity. Additionally, they have been proven to increase apoptosis in cancer cells. and cytotoxicity in both 2D and 3D cell culture models. These findings imply that PGPLs may be an effective nano-formulation for the management of PDAC. However, further research and clinical trials would be necessary to determine their efficacy and safety in humans.

2.8 Pancreatic Cancer Treatment Using Rosette Nanotubes as a Novel and Successful siRNA Delivery Vehicle

It is interesting to note that RNTs have been found to be promising nanocarrier for delivering therapeutic RNA payloads to pancreatic cancer cells. RNTs are biocompatible and have tunable physical, chemical, and biological properties, making them versatile drug delivery vehicles. This study specifically showed that RNTs were effective in silencing oncogenes in an in vitro model of pancreatic ductal adenocarcinoma (PDAC) using siRNA targeted against KRAS. The RNT delivery system's effectiveness in delivering siRNA and performing its intended function could be seen and verified through the use of fluorescently tagged siRNA. Overall, this study highlights the potential Delivering therapeutic RNA payloads to cancer cells with specificity using RNTs as a nanocarrier. More investigation is required to determine the effectiveness and safety of RNTs in vivo and to optimize their properties for clinical use.

2.9 Undaria Pinnatifida fucoidan-based bioactive targeted nanoparticles

Fucoidan, a brown algae-derived marine polymer, as a treatment for pancreatic cancer, which is among the most life-threatening types of cancer. The researchers suggested converting the polymer to nanoparticles to enhance its activity against cancer cells and improve its passage through the stroma around the pancreatic cancer. To achieve this, utilising the polyelectrolyte interaction with lactoferrin, a positively charged, active targeting ligand, they created unique fucoidan-based nanoparticles.The polymer was also shown to have the capacity to lessen the tendency of the movement of pancreatic cancer cells and attack, which are the primary causes of the virulence of this kind of cancer. Next, interactions between the positively charged protein lactoferrin and polyelectrolytes were used to test the polymer's ability to create nanoparticles. An optimum formulation of the produced particles had a size of 167 nm and a negative surface charge of 27 mv after being optimised.The particles could maintain their integrity in an acidic environment and showed prolonged fucoidan release. On PANC-1 cells, the effectiveness of blank nanoparticles in preventing cancer was assessed.and they revealed a 2.3-fold reduction in the polymer's IC50 value. Cancer cell invasion and migration were inhibited to a greater extent by the particles.The study emphasises the possibility of adopting this innovative nanosystem as a secure, all-natural therapy for pancreatic cancer. A six-month term of lyophilized powder storage of the particles also revealed satisfactory stability.

2.9.1 Gene silencing nanomedicines

Nanomedicines that silence genes offer enormous potential in order to combat pancreatic cancer. Pancreatic cancer is a dangerous one that frequently discovered at an advanced stage and is difficult to treat. Gene silencing nanomedicines can target specific genes, a factor in the occurrence and spread of pancreatic cancer, and can inhibit their expression, thereby blocking the expansion and dissemination of cancer cells. One example of nanomedicines that silence genes to cure pancreatic cancer is siRNA-based therapeutics. SiRNA

is a short RNA molecule that can bind to specific mRNA sequences and cause their degradation, resulting in the silencing of the targeted gene. Researchers have developed siRNA-based nanomedicines that can target genes involved in pancreatic cancer, such as KRAS and P53.

Gene silencing nanomedicines are developed and evaluated using a variety of models. These models may be used to investigate the efficacy, safety, drug kinetics, and pharmacodynamics of gene silencing nanomedicines for the treatment of pancreatic cancer.

- The cellular absorption, intracellular transport, and gene silencing activities of nanomedicines are investigated using in vitro models. In these models, pancreatic cancer cell lines are cultured, subjected to gene silencing nanomedicines, and their effects on gene expression, cell growth, and apoptosis are assessed. Nanomedicines' immunogenicity and toxicity can also be investigated utilising in vitro modelling.
- In vivo models are used to study biodistribution, pharmacokinetics, and efficacy of nanomedicines in animal models of pancreatic cancer. These models involve the injection of nanomedicines into mice or rats using xenograft tumours created from patient-derived tumours or pancreatic cancer cell lines.. In vivo models can be used to evaluate the tumor-targeting ability, therapeutic efficacy, and safety of nanomedicines.
- Transgenic mouse models are used to study the function of certain genes in the onset and spread of pancreatic cancer and to evaluate the effects of gene silencing nanomedicines on tumor growth and metastasis. These models involve the genetic modification of mice to express or knockdown specific genes involved in pancreatic cancer, followed by the injection of gene silencing nanomedicines to study their effects on tumor development and progression.

In general, the use of these models enables researchers to learn more about the therapeutic potential and mechanisms of action of silenced gene nanotechnology in the management of pancreatic cancer.

III. SOME POTENTIAL FUTURE RESEARCH AREAS TO DEVELOP TREATMENTS FOR PDAC INCLUDE

1) **Stromal modulation:** Instead of depletion, stromal modification of the pancreatic tumour microenvironment (TME) may improve the administration of chemotherapeutics and make the tumour more susceptible to immune checkpoint blockade drugs. Anti-stromal medications, such the angiotensin II receptor antagonist Losartan, have demonstrated potential in stromal and vascular remodelling.

2) **Polymer design and chemistry:** The creation of adaptable polymeric delivery systems for immunological adjuvants and tumor-associated antigens (TAAs) has been made possible by developments in polymer design and chemistry. By promoting cytosolic transport, these approaches assist with antigen cross-presentation and give molecular targeting abilities to PDAC immunotherapies, enabling more intelligent drug development.

3) **Nano-enabled strategies:** Combining the delivery of chemotherapeutic agents, small molecule medicines, and gene therapy can enhance PDAC sensitization to treatment. By allowing synergies in terms of co-delivery of different payloads, targeting abilities, and theranostic activity, multifunctional NPs with diverse and complimentary functioning might improve the efficacy of PDAC therapies.

4) **EVs and exosomes:** Targeted treatments are being thought of as having an alternative natural delivery method that uses extracellular vesicles (EVs) and exosomes. Exosome delivery with the development of molecular and nanobiosensors may lead to the development of a non-invasive, very sensitive, and precise diagnostic tool for PDAC.These fields of study have the potential to greatly raise patient survival rates for PDAC, which continues to be one of the most deadly and challenging forms of cancer in people.

IV. FUTURE CHALLENGES AND PROSPECTS FOR NANOCARRIERS IN PANCREATIC CANCER

Nanocarriers hold immense potential as a tool for targeted drug delivery in pancreatic cancer. However, they must overcome a number of challenges inorder to realise all of their abilities:

1. **Specificity and targeting:** Nanocarriers need to be specifically designed to target pancreatic cancer cells while minimizing the impact on healthy cells. Understanding the cellular and genomic characteristics of the tumour microenvironment is essential for this.

2. **Drug loading and release:** Ensuring that drugs are loaded onto the nanocarrier effectively and released at the right time and place is critical for effective treatment.

3. **Stability and circulation time:** Nanocarriers need to be stable in circulation to effectively reach the tumor site. This requires consideration of the physiochemical properties of the carrier and the external environment.

4. **Toxicity:** To make sure that they do not unintentionally injure the patient, the safety of nanocarriers must be thoroughly assessed.

Despite these challenges, nanocarriers have great potential in the pancreatic cancer therapy. Some of the prospects of nanocarriers include:

1. **Personalized medicine:** Nanocarriers can be designed to target specific mutations or biomarkers present in individual tumors, allowing for personalized treatment approaches.

2. **Combination therapies:** Nanocarriers can be loaded with multiple drugs or drug combinations, allowing for more effective treatment strategies.

3. **Improved pharmacokinetics:** Nanocarriers can extend the circulation time of drugs, allowing for better drug delivery and a reduction in required dosages.

4. **Overcoming drug resistance**: Nanocarriers can potentially overcome drug resistance by delivering drugs to specific targets within cells.

Overall, the prospects for nanocarriers in the pancreatic cancer therapy are exciting, and continued research in this area is likely to yield significant advances in cancer therapy.

V. CONCLUSION

The review recommends adopting novel drug delivery methods and competent methodologies for the treatment of pancreatic cancer, as well as integrating nanotechnology-based strategies into and alongside immunotherapy, gene therapy, radiation, and other related therapeutic treatments. An effective strategy for managing pancreatic cancer may combine tumour targeting with novel modes of localized medication delivery techniques. Consequently, the problem of localization and site-specific administration can be addressed by new carrier-mediated formulations containing anti-cancer medications. Such delivery methods can stop the growth of cancer cells and effectively trigger their apoptosis. Recent data from in vivo and/or in vitro studies indicate, nanotechnology platforms have become a promising technique in the treatment of pancreatic cancer. However, in terms of future toxicity and targeted tumour tissue delivery, additional study is required before these reported nanocarriers may be employed in clinical applications for the treatment of pancreatic cancer metastasis or PDAC. In a nutshell, new and enhanced medication delivery methods hold great promise for the effective and quick treatment of pancreatic cancer.

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