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Review on Noval Anticancer Drug

Miss. Ashwini Gaikwad R , Prof. Sayyad. J. H, Miss. Badakvaishnavi P,
Miss. Agrwal Nandini H. and Mr. Akolkar Ganesh. G
Rashtriya College of Pharmacy, Hatnoor, Kannad, Sambhajinar, Maharashtra, India

Abstract: *Paclitaxel is One of the most significant lead compound to come from a natural source is paclitaxel. Paclitaxel is mostly derived from the bark of a slow-growing Western yew because to its unique and complex chemistry. Even if paclitaxel's complete chemical synthesis has been accomplished, it might not be financially viable. The paclitaxel has a minimal therapeutic index: it is nearly insoluble in water and extremely lipophilic. The injection that is sold commercially preparation is a sterile mixture of dehydrated alcohol and the medication in Cremophor. Current cancer Hypersensitivity responses are common when paclitaxel is used in chemotherapy. Taxol, also known as paclitaxel, is frequently used in clinical settings to treat a range of malignancies. It needs ethanol and Cremophor EL(polyethoxylated castor oil) as a carrier due to its poor water solubility. When administered intravenously, these substances result in severe allergic responses. Paclitaxel was covalently bonded to human serum albumin in this investigation. TheAfter succinic anhydride was used to esterify the drug's 29-hydroxyl group, it was derivative to yield the N-hydroxy-3-sulfo-Succinimide active ester, which reacts strongly with the protein's lysyl amino groups. Two distinct populations of conjugates (with six orEach albumin molecule has 30 average drug molecules attached to it, which were produced, purified, and described. The conjugations were stable in serum and physiological solution, however the addition of liver extract or proteases caused . paclitaxel is used in the chemotherapy treatment for breast cancer and ovarian cancer.*

Keywords: Introduction of paclitaxel, essential properties, MOA of paclitaxel, Analytical methods of paclitaxel, uses of Paclitaxel

I. INTRODUCTION

Paclitaxel is nearly insoluble in water and has a low therapeutic index due to its high lipophilic. A sterile solution of the medication in Cremophor EL and dehydrated alcohol makes up the commercially available injectable preparation. paclitaxel is primarily taken from the bark of Western yews, which grow slowly.

Despite Although paclitaxel's complete chemical synthesis has been accomplished, it might not be commercially viable[1]. The paclitaxel has a minimaltherapeutic index: it is nearly insoluble in water and extremely lipophilic. The injection that is sold commercially preparation is a sterile medication solution in dehydrated alcohol and Cremophor® EL: The significance of creating a better delivery systemThe issues with the paclitaxel system are clear[2].

In the 1960s, the National Cancer Institute's screening and discovery program for novel cancer treatments included the development of paclitaxel.

In thisa number of plant extracts were examined for antitumor properties, including a crude extract from Taxes bre6ifolia's bark (Pacific orWestern yew. When tested against multiple cancer cell lines, this crude extract demonstrated anticancer efficacy andthe active ingredient's chemical makeup of Paclitaxel was discovered as the extract No additional chemotherapeutic substance other than than penicillin has attracted a lot of attention as Paclitaxel's distinct mechanism of action was (Paclitaxelis among the most crucial lead substances to originate in the natural world [3]

Globally, cancer is regarded as one of the most dangerous diseases. Even with the quick development of novel treatment strategies, cancerous tumors remain among the top causes of mortality worldwide.

Over the last few For many years, the traditional method of treating cancer has included radiation, surgical excision, and chemotherapy. However, chemotherapy and radiation lower quality of life because to their toxicity and severe adverse effects[4].

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Additionally, they are at danger of making cancer cells resistant so they are unaffected by radiation and chemotherapy. Consequently, these challenges and Reaching the intended patient outcomes has been difficult. challenging; as a result, researchers are now looking for innovative indigenous therapies.
Lately, the anti-cancer characteristics of Numerous natural substances have been found, leading to their application[5]

1) Essential properties of paclitaxel
Nanomedicine
Particle size
For the therapy of cancer, the optimal nanomedicine diameter is between 10 and 100 nm. Because nanomedicine particles cannot be too small or they would be rapidly eliminated by the kidneys, the glomerular wall's sieving coefficient establishes the range of particle sizes. Tumors have pores that range in size from 380 to 780 nm, although particles smaller than 2 nm can typically pass through the vasculature. Submicron particles have been shown to enhance the medication penetration and retention impact by concentrating in tumors after leaking out of the bloodstream[6]

2) Properties of pharmacokinetics
Regarding pharmacokinetics, paclitaxel is poorly soluble in water and has a high molecular weight of 853.0 g mol-1. Its primary metabolite, 6a-hydroxypaclitaxel, is produced by CYP2C8, whereas two lesser metabolites are produced by CYP3A4. The pharmacokinetics of this medication exhibit a significant standard variability, and the often recommended dosage is 200–250 mg/m2, administered as an infusion across 3 and 24 hours.[7]
The steady-state volume of distribution was determined to be around 87.1 mL/min/m2, and the terminal half-life was reported to be between 1.3 and 8.6 h (mean 5 h) Less than 10% of the drug is eliminated in the urine in its unaltered form due to the drug's substantial hepatic metabolism mediated by P-450 (isoenzyme CYP3A and CYP2C) . Over 90% of PTX binds to plasma proteins quickly and extensively, and the majority of the medication is eliminated in the feces . The areas of rats with the highest drug concentrations were the lung, liver. When administered for 6–24 hours, it undergoes biliary excretion with a 5.8-hour elimination half-life.39 It is dispersed in ascitic fluid but does not cross the blood–brain barrier.[8]

3. Breast Cancer Chemotherapy
As previously said, BC is a diverse illness with unique characteristics. Finding the BC subtypes is essential to choosing the right chemotherapy medications. Chemotherapeutic medications are divided into classes based on their method of action, such as antimetabolites, immunologic therapy, endocrine therapy, DNA alkylating agents, and antimitotic medications . The induction of apoptosis during the synthesis phase is caused by antimetabolites. Antimetabolites' structures are similar to those of purines, pyrimidines, or folate and lead to errors during replication. [9]

Stages of cancer
0 stage cancer: Although there are aberrant cells, they haven't proliferated. Precancerous cells can also be referred to as stage 0.The majority of stage 0 malignancies can be cured.
stage I cancer: The tumor is smaller and localized. No other parts of your body or adjacent lymph nodes have been affected.
stage II: The tumor has gotten bigger and may have reached neighboring lymph nodes.
Stage III cancer: The tumor has migrated to neighboring lymph nodes and has gotten deeper into the surrounding tissues.
Stage IV cancer: This type of cancer has metastasized, or spread, to other organs or remote parts of the body. Another name for this is metastatic cancer [10].

The Mechanism of Action of Paclitaxel
The Polymerization Factor of Paclitaxel By encouraging the synthesis of alpha and beta tubulin subunits, which are the building blocks of microtubules, PTX binds to microtubules rather than tubulin dimers and stabilizes microtubules (polymerization) .

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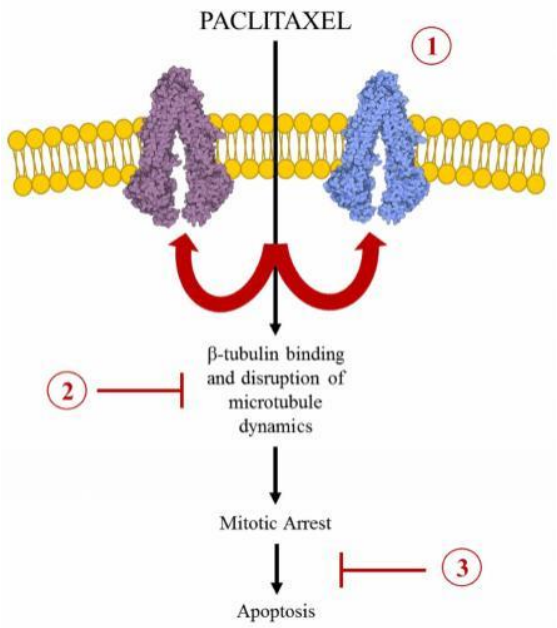
The medication lengthens the tubulin polymer by lowering the critical concentration of tubulin needed for its assembly . The dynamics of microtubules are hampered by their stability. Cell division subsequently stops at the G2 or M phase as a result of the mitotic checkpoint's inadequate requirements, which interfere with the cell's capacity to divide [11].Even calcium and cold temperatures have no effect on the polymerized and stable microtubules. Because calcium decreases PTX's affinity for tubulin, the balance of polymerization and depolymerization moves in the direction of the equilibrium of polymerization/depolymerization shifts in favor of polymerization to counteract the effect of calcium decreasing PTX's affinity for tubulin [12].Furthermore, chondrocytes demonstrate that PTX results in cytoskeletal abnormalities, where microtubules in the cytoplasm become straight and stubby, with a rough endoplasmic reticulum, in contrast to the control group's delicate, sinous filaments. These alterations last for 48 hours following PTX withdrawal. The modified microtubules fuse adjacent endoplasmic reticulum complexes together and remove ribosomes from the rough endoplasmic reticulum [13].

Only free microtubules that are not joined to or already present in the microtubule organizing centers (MT) are polymerized by PTX.The first microtubule-stabilizing drug discovered, paclitaxel is regarded as the most important development in chemotherapy over the previous 20 years.The primary building blocks of the cytoskeleton are long, filamentous, tube-shaped protein polymers called microtubules. Since they are involved in cell signaling, intracellular transport, cell division and mitosis, and the development and maintenance of cell shape, they are vital to all eukaryotic cells[14]. Slender filamentous tubes made up of α-tubulin and β-tubulin heterodimers make up microtubules. Antimicrotubule medicines are medications that change how microtubules behave. These medications are typically divided into two categories. Microtubule polymerization is inhibited by one type of chemical called a microtubule-destabilizing agent. The second primary kind Is referred to as the paclitaxel and other microtubule-stabilizing medicines[15]. Paclitaxel attaches itself to the microtubule's β-tubulin subunit's N-terminal 31 amino acids . In both differentiated and undifferentiated Nl15 cells, it promotes β-tubulin phosphorylation . Cell death results from this binding's stabilizing effects and increased microtubule polymerization . Paclitaxel stabilizes microtubules and stops somatic cell mitosis at the G2/M stage of replication, according to research done in 1992 by Horwitz and colleagues [16].



Fig(1). Mechanism of action of paclitaxel.

Changes to tubulin, the taxanes' biological target, are the main mechanism of cancer resistance. Mutations, tubulin isotype selection, and post-translational changes in tubulin and related regulatory proteins are examples of these modifications.

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Development of resistance

Overexpression of the ATP-binding cassette (ABC) transporters, changes in the binding regions of β-tubulin and tubulin mutations, decreased function of important apoptosis proteins (like Bcl-2 and p53) , changes in cytokine expression (like Interleukin-6), and CYP-mediated paclitaxel detoxification are some of the cellular and molecular mechanisms causing paclitaxel resistance[17].The ABC transporters are energy-dependent transporters that penetrate cell membranes and use ATP hydrolysis to move substrate between cells . Increased ABC transporter expression caused anticancer drugs to efflux (pumping the drug out of the cell), which decreased their effectiveness and paved the way for the emergence of multidrug-resistant (MDR) cells. ABCB1 encodes the membrane protein P-glycoprotein (P-gP), which is a member of the ABC transporter family [18].

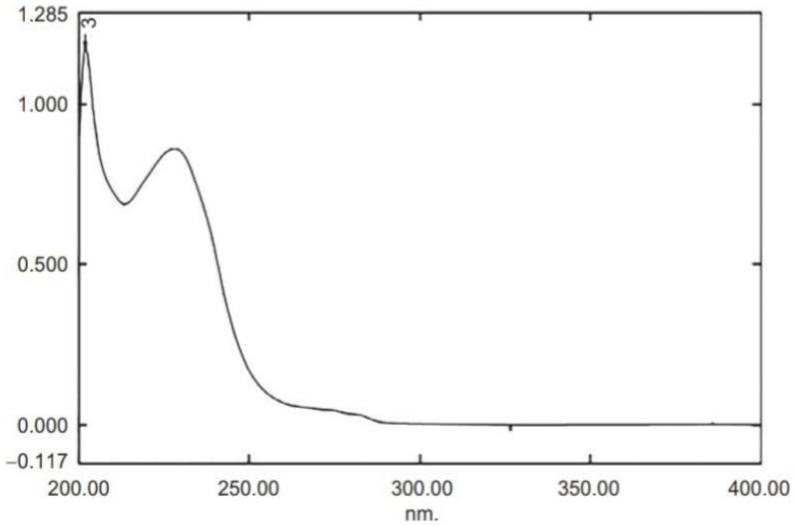
Management

Paclitaxel's hydrophobicity, poor aqueous solubility, and low oral bioavailability make delivery difficult . Cremophor EL, a solubilizer intended to improve solubility, is a component of commercially marketed paclitaxel formulations. Cremophor EL has a molecular weight of about 3 kDa and is a white to off-white viscous liquid Hypersensitivity responses, hyperlipidemia, and peripheral neuropathy, including axonal degeneration and demyelination, are caused by the inclusion of the Cremophor EL in the formulation [19].By Ureversing P-gP activity, Cremophor EL has been shown to increase the effectiveness of paclitaxel in a multidrug-resistant cancer cell line .Hepatotoxicity, hypersensitivity, neurotoxicity, alopecia, myopathy, exhaustion, and pulmonary lipid embolism are additional frequent toxicities linked to paclitaxel [20].

Spectroscopy

Spectroscopy of UV

Using a UV/VIS spectrometer the ultraviolet absorption spectrum of paclitaxel in methanol was scanned between 200 and 400 nm. The results are displayed in. Fig.1 It was discovered that paclitaxel has a maximum absorption at 228 nm[21].



Fig(2). UV spectrum of paclitaxel in methanol

HPLC or high performance liquid chromatography

The most popular analytical technique for separating and determining paclitaxel from plant extracts, raw materials, and various pharmaceutical dosage forms is high-performance liquid chromatography (HPLC).

New high performance liquid chromatography-mass spectrometry (HPLC-MS) methods for quantifying paclitaxel from aqueous, protein, and oil-containing materials were created and verified by Turner .The Waters Symmetry C-18 column

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and a mobile phase consisting of 0.1% acetonitrile-water and formic acid (45:55, v/v) with isocratic flow at 200µL/min were used for the experiment.

The literature has detailed a number of analytical techniques for quantifying PTX in various matrices.[22]

These techniques include, for example, immunoassays, tubulin-based biochemical tests, micellar electrokinetic chromatography (MEKC), and chromatography-based assays, which are covered in the following areas. The majority of methods use high-performance liquid chromatography (HPLC) in conjunction with a UV or MS detector, presumably because of its increased sensitivity and resolution and capacity to work with various matrices, which aids in analyses where interference and matrix effects may be present.[23]

Micelles serve as a pseudo-stationary phase in a solution in this separation technique, which is typically used in conjunction with a UV detector to measure the signal response. MEKC has a higher LLOQ (lower limit of quantification) than most HPLC-UV analyses because it requires a smaller sample volume. Nevertheless, this method uses less solvent waste and produces good results if the matrix contains taxines, a toxic alkaloid compound isolated from taxus spp., preventing collating issues that arise in HPLC.[24]

Suggested a different approach for everyday use by comparing the measurement of paclitaxel in liposomal formulation using first-derivative spectrophotometry with ultraviolet detection (DS-UV) and HPLC methods. The DS-UV technique was created with a 2 nm bandwidth and a 200–400 nm wavelength range. The amplitude was measured at 246 nm using the zero-crossing wavelengths in the absorbance spectra's first derivative. In the validation trial, there was no discernible difference between the HPLC-UV results and this method. In contrast to HPLC-UV, DS-UV offered a quick, easy, and affordable alternative approach [25].

Drug delivery system

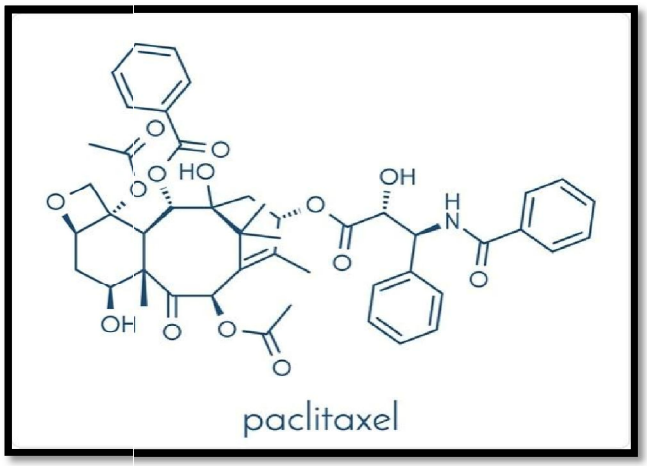
Systems for delivering drugs

Liposomes, polymeric nanoparticles, micelles, dendrimers, inorganic nanoparticles, carbon nanotubes, hydrogels, and cyclodextrin nanoparticles are a few of the delivery mechanisms that can be used for PTX loading. Because of their many benefits over conventional therapy, Nano carriers have garnered more interest recently, particularly for cancer treatments.

Due to their small size and the permeability and retention (EPR) effect, nanoparticles can increase the solubility of this medication. Additionally, they can evade the reticuloendothelial system's (RES) recognition due to steric hindrance brought on by PEGylation, which lessens the drug's side effects and enhances the pharmacokinetic profiles of the drug from nan carriers.[26]

Appearance

Paclitaxel is available as a white to off-white crystalline powder.



Fig(3). Structure of paclitaxel

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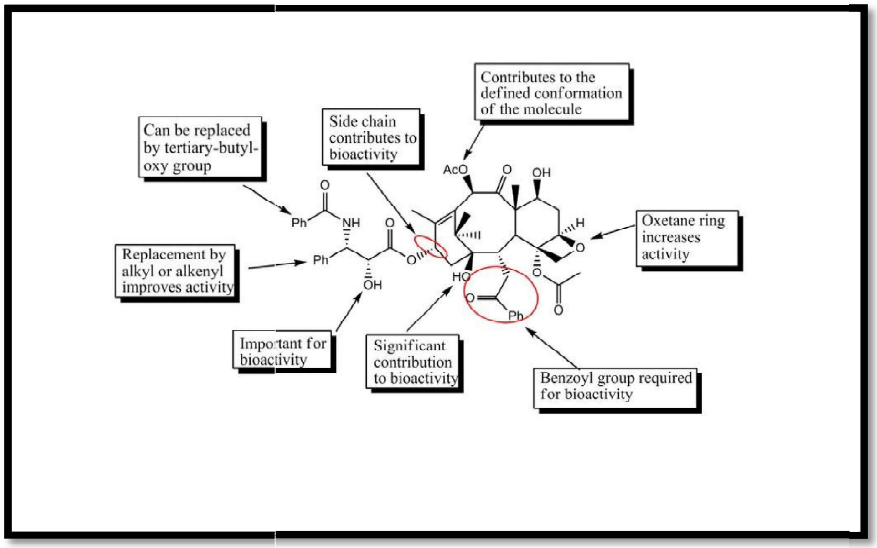
SAR of Paclitaxel



Applications and uses

One of the most popular antineoplastic drugs, paclitaxel exhibits extensive action against a variety of malignancies, such as cervical carcinoma, non-small-cell lung cancer, breast cancer, endometrial cancer, and bladder cancer [27].

• **ovarian cancer :**The US Food and Drug Administration (FDA) authorized paclitaxel in 1992 for the treatment of ovarian cancer and in 1994 and 1999 for the treatment of advanced and early-stage breast cancer, respectively.[28]

• **Advanced ovarian cancer:** is initially treated with a combination of paclitaxel and a platinum-containing substance (cis-platin or carboplatin). When traditional therapy is ineffective for treating metastatic ovarian cancer, paclitaxel alone is employed.[29]

•**Metastatic bladder cancer:**To treat metastatic or advanced bladder cancer, paclitaxel and gemcitabine are used.[30]

•**Advanced cervical cancer:** Paclitaxel is used to treat advanced cervical cancer in conjunction with topotecan, bevacizumab, andor cisplatin.[31]

•**Esophageal and gastric cancers:** When paired with carboplatin and radiation treatment, paclitaxel is an essential part of preoperative care for patients with these types of tumors.[32]

• **Anaplastic thyroid cancer:** Paclitaxel is a treatment option for this type of thyroid cancer.[33]

• **Advanced head and neck cancer:** Cisplatin and paclitaxel are used together to treat advanced head and neck cancer.[34]

Development of resistance

Overexpression of the ATP-binding cassette (ABC) transporters, changes in the binding regions of β-tubulin and tubulin mutations, decreased function of important apoptosis proteins (like Bcl-2 and p53) , changes in cytokine expression (like Interleukin-6), and CYP-mediated paclitaxel detoxification are some of the cellular and molecular mechanisms causing paclitaxel resistance. The ABC transporters are energy-dependent transporters that penetrate cell membranes and use ATP hydrolysis to move substrate between cells [35].

Increased ABC transporter expression caused anticancer drugs to efflux (pumping the drug out of the cell), which decreased their effectiveness and paved the way for the emergence of multidrug-resistant (MDR) cells. P-glycoprotein (P-gP), a membrane protein and well-known efflux pump that causes MDR, is encoded by ABCB1, a member of the ABC transporter family. Paclitaxel-resistant cells displayed elevated P-gP levels and cross-resistance to other hydrophobic medications . In addition to the efflux pump, changes in microtubule dynamics or composition are another route of paclitaxel resistance. Recent research has demonstrated that paclitaxel resistance results from overexpression of β III-tubulin, which decreases paclitaxel's capacity to inhibit microtubule dynamics [36].

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Administration

Paclitaxel's hydrophobicity, poor aqueous solubility, and low oral bioavailability make delivery difficult.Cremophor EL, a solubilizer intended to improve solubility, is a component of commercially marketed paclitaxel formulations. Cremophor EL has a molecular weight of about 3 kDa and is a white to off-white viscous liquid.Hypersensitivity responses, hyperlipidemia, and peripheral neuropathy, including axonal degeneration and demyelination, are caused by the inclusion of the Cremophor EL in the formulation . By reversing P-gP activity, Cremophor EL is found to increase the effectiveness of paclitaxel in a multidrug-resistant cancer cell line[37]. Hepatotoxicity, hypersensitivity, neurotoxicity, alopecia, myopathy, exhaustion, and pulmonary lipid embolism are additional frequent toxicities linked to paclitaxel . Paclitaxel's poor solubility, bioavailability, and toxicity make it necessary to design a delivery strategy that can lower systemic toxicity while enhancing safety and effectiveness. To address the limitations of Cremophor EL in the formulation, several paclitaxel administration methods without Cremophor EL were also studied. Pastes, liposomes, micelles, nanospheres, cyclodextrin complexes, emulsions, prodrugs, and macromolecular adducts are some examples of these delivery systems[38].

Pastes

In order to include greater concentrations of the water-insoluble medication in a fatty base, paclitaxel paste formulation was taken into consideration [51]. A polymeric surgical paste was created in the Winternitz et al. trial by mixing 1–30% w/w of paclitaxel with PCL (polycaprolactone) and Me PEG (methoxy poly-ethyleneglycol). Ten to fifteen percent of paclitaxel was released during a three-week period, according to the in vitro drug release experiments. When 20% w/w paclitaxel paste was injected into MDAY D2 solid tumor-bearing mice, there was a complete suppression of tumor regrowth.The release of paclitaxel from PCL paste has increased with the addition of gelatin, dextrin, and sodium chloride [39].

Liposomes

Over the past ten years, liposomal formulation for paclitaxel has been thoroughly studied and refined in an effort to prolong drug release, improve cellular absorption, and remove Cremophor EL from formulation. In an animal model, the liposomal formulation of paclitaxel demonstrated comparable anti-tumor activity and reduced toxicity to the therapeutic formulation

Both paclitaxel-loaded cationic liposomes (EndoTAG®-1, Medigene) and liposome-entrapped paclitaxel (LEP-ETU, NeoPharm) have advanced to phase II of clinical studies and demonstrated encouraging outcomes.like Pharmaceutical (Nanjing, Jiangsu, PRC) created the other liposomal-paclitaxel mixture (Lipusu®), which was authorized by the Chinese State FDA and effectively utilized in China. [40].

Nanospheres

Because of their small particle size, nanospheres can be administered systemically, locally, and orally. The majority of nanospheres are typically made with biodegradable and biocompatible polymers. They are employed as a delivery mechanism to improve drug trapping and release.[41]

The study by Feng et al. used poly(D,L-lactic-co-glycolic acid) (PLGA) and poly(D,L-lactic acid) polymers to create paclitaxel-loaded nanospheres.Paclitaxelnanospheres were successfully prepared from biodegradable polymers coated with phospholipids, cholesterol, and vitamin E TPGS (tocopherol polyethylene glycol succinate) in a number of investigations [42].

In PLGA-paclitaxel nanospheres, it has been demonstrated that using dipalmitoyl-phosphatidylcholine (DPPC) as an emulsifier produced more advantages than PVA. The TPGS may considerably increase the paclitaxel's encapsulation efficiency in PLGA nanospheres when compared to PVA.According to Perkins et al., paclitaxel nanospheres coated with PEG 5000 and distearoyl phosphatidylethanolamine had a longer circulation time.research by Sharma et al. shown that in a model of cancer-induced mice, polyvinylpyrrolidoneNano spheres encapsulating paclitaxel extended survival time. [43]

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Nanoparticles

Potential pharmacological advancements in cancer treatment have been demonstrated by the use of nanoparticles for drug delivery. The FDA authorized albumin-boundAbraxane, a paclitaxel nanoparticle, will be administered to individuals with metastaticNSCLC (non-small-cell lung cancer) and breast cancer.ThesePaclitaxel nanoparticles are 130 nm albumin-bound particles thatIs demonstrated to be less harmful and more effective because of improved performance.Effect of mobility and retention (EPR).. They attach to the gp60 receptor onEndocytosis and alveolar transport to penetrate the endothelium barrier.Transportation [44].

Further more albumin-paclitaxel complexes attach themselves to the secretedThetumor interstitial space contains the protein SPARC, which is acidic and rich in cysteine.Area that facilitates medication penetration and targeting in malignancies .Various polymers, including PLA, PLGA, and chitosan, were utilized for preparation.

Arationpolymeric nanoparticles of paclitaxel . As an example, earlierResearch revealed that PLGA nanoparticles loaded with paclitaxel were prepared using many techniques. [45]

Prodrug

Paclitaxel prodrugs are utilized to increase water solubility, boost efficacy, and do away with the need for Cremophor EL. Prodrugs are ester derivatives made using paclitaxel's alcoholic functional group at either position C-2 or C-7 These prodrugs have demonstrated cytotoxic activity against cancer cell lines in smaller tumor that is comparable to paclitaxel.Higher aqueous solubility was demonstrated by the synthesized PEG paclitaxel prodrug . In a different study, PEG (MW 5000) was conjugated with the prodrug paclitaxel and showed equivalent in vitro cytotoxicity to paclitaxel in B16 melanoma cells, along with better solubility

Furthermore, in a P388 murine leukaemia model, PEG-conjugated paclitaxel-2-glycinate was found to have greater anticancer effectiveness and lower toxicity in comparison to Taxol. Accordingly, it was shown that this prodrug was active against mice with solid tumours that were HT-29, A549, and SKOV3 [46].

Emulsions

In recent years, emulsions and other alternative drug delivery systems have been developed to solubilize paclitaxel and lessen its toxicity by removing Chromophore EL from its composition. For example, a vitamin E-based paclitaxel emulsion called TOCOSOL® paclitaxel has been developed . Ethanol and Cremophor EL were removed from this formulation.

In both B16 and HCT-15 tumor-bearing mice models, the TOCOSOLTM formulation significantly improved the antitumor activity when compared to Taxol (commercially available pacli-taxel)

However, all of the TOCOSOLTM phase III clinical trials have shown a similar objective response rate to Taxol in women with metastatic breast cancer.[47]

However, all of the TOCOSOL™ phase III clinical trials were shut down due to the similar objective response rate of TOCOSOL™ to Taxol in women with metastatic breast cancer.

In another trial, paclitaxel was formulated in an o/w emulsion with glycerol, phosphatidylcholine (EPC), Tween 80, and an oil blend (tricaproin, tricaprylin, and tributyrin). In a mouse model with an intraperitoneal S-180 tumor, this formulation significantly extended the mice's lifespan when compared to Taxol. Two microemulsion systems, LBMW (lecithin:buta-nol:myvacet:water) and CMW (capmul:myvacet:water), were developed and Chow as paclitaxel delivery methods [48].

When compared to Taxol, the LBMW and CMW formulations showed a 25% and 50% longer release of paclitaxel, respectively. Studies conducted in vivo showed that[68].Both formulations demonstrated a longer circulation duration and a higher blood plasma concentration of paclitaxel, according to in vivo experiments. An oral o/w nano-emulsion containing paclitaxel was created by another study team using egg lecithin as the main emulsifier, pine nut oil as the oil phase, and stearyl amine and deoxycholic acid to adjust the positive and negative charges, respectively . Following oral administration of this nan emulsion, increased paclitaxel bioavailability was noted. The same research team created a nan emulsion formulation three years later that contained curcumin and paclitaxel [49].

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Stability

Solution stability In polyolefin, low-density polyethylene, and glass containers, paclitaxel at a concentration of 0.3 mg/mL in 0.9% sodium chloride was stable for 13, 16, and 13 days at 2–8°C; in 5% glucose, it was stable for 13, 18, and 20 days, respectively . In poly-olefin, low-density polyethylene, and glass containers, the solution containing 1.2 mg/mL of paclitaxel in 0.9% sodium chloride remained stable for 9, 12, and 8 days at 2–8°C; in 5% glucose, it remained stable for 10, 12, and 10 days, respectively. The paclitaxel solution All diluent/container combinations showed stability at 0.3 and 1.2 mg/mL concentration for three days at 25°C, with the exception of 5% glucose In glass, which showed stability for seven days, and 1.2 mg/mL concentration in 0.9% sodium chloride for five days[50].

II. CONCLUSIONS AND PROSPECTS FOR THE FUTURE

One of the best anticancer medications ever created is PX. It works effectively against a variety of malignancies. However, there are problems with the usage of ethanol and Cremophor EL in the present Taxol formulations. Nanotechnology is a very active research area in both academic and industrial settings because nano-delivery systems may be free of ethanol and Cremophor EL, improve PX pharmacokinetic profiles in vivo, increase PX solubility, decrease its side effects, and passively or actively target to tumor sites due to the EPR effect and the use of targeting ligands, respectively.

As a result, a variety of PX nano-delivery systems have been created, including lipid-based formulations, polymeric nanoparticles, inorganic nanoparticles, polymer conjugates, carbon nanotubes, nanocrystals, and cyclodextrin nanoparticles. There are several new PX NP formulations undergoing clinical trials, and the FDA has so far approved PX albumin-bound NPs (Abraxane®) for the treatment of metastatic breast cancer and non-small cell lung cancer.

Frequency of myelosuppression, hypersensitivity responses, etc. It's unclear, though, if these novel formulations would increase survival.

Despite the fact that nano-delivery technologies have been shown to be viable and promising in cancer treatment, there are numerous obstacles that prevent their widespread use.

Despite the fact that nano-delivery technologies have been shown to be viable and promising in cancer treatment, there are numerous obstacles that prevent their widespread use.

First, it is challenging to completely describe the physicochemical characteristics of NP systems, and each NP delivery system appears to be distinct. In connection with this, producing NP on a wide scale will present additional difficulties. Second, there is a paucity of knowledge on the stability of NP formulations and the mechanisms of drug release from them in vivo, as well as the overall fate of the drug and its vehicles in the human body.

Numerous analytical techniques for quantifying paclitaxel in a variety of matrices, including as biological matrices and delivery systems, have been documented in the literature. Immunoassays, such as LC-MS/MS, have good sensitivity and selectivity among these techniques; however, their use is limited by the time required for pre-treatment.

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