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"From Tree To Therapy: A Review Of Paclitaxel's Development, Mechanistic Pathways, And Analytical Monitoring Approaches."

V. Sravan Kumar [1*], P. Srinivas Babu[2], Sk. Asif Ali[1], T. Aiswarya[1], M. Sarah[1], M. Pallavi[1], D. Sandhya[1].

1.Department of Pharmaceutical Chemistry, Vignan Pharmacy College, Vadlamudi, 522213, Andhra Pradesh, India.

2. Department of Pharmaceutics, Vignan Pharmacy College, Vadlamudi,522213, Andhra Pradesh, India.

Abstract:

Paclitaxel, a prominent chemotherapeutic agent originally derived from *Taxus brevifolia*, has garnered extensive scientific and clinical interest due to its unique mechanism of action and broad-spectrum antineoplastic activity. This comprehensive review delves into the fundamental characteristics of paclitaxel, including its physicochemical properties, mechanism of action, and pharmacokinetics. Special emphasis is placed on its distinctive ability to stabilize microtubules, thereby disrupting cell division and inducing apoptosis in cancer cells. The review also explores the challenges associated with paclitaxel's solubility and bioavailability, which have led to the development of novel formulations and delivery systems. Furthermore, it highlights recent advances in analytical techniques used for the qualitative and quantitative assessment of paclitaxel in various matrices. Techniques such as high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC-MS), and emerging nanotechnological methods are critically examined. By consolidating insights from recent literature, this review aims to provide a robust foundation for researchers, clinicians, and pharmaceutical developers working on paclitaxel-based therapies or analytical innovations.

Keywords: Paclitaxel, microtubule stabilization, anticancer drugs, analytical methods, HPLC, LC-MS, drug delivery, pharmacokinetics, formulation development, nanotechnology.

Introduction:

Paclitaxel, sold under the brand name Taxol among others, is a chemotherapy medication used to treat ovarian cancer, oesophageal cancer, breast cancer, lung cancer, Kaposi's sarcoma, cervical cancer, and pancreatic cancer. It is administered by intravenous injection. There is also an albumin-bound formulation. Common side effects include hair loss, bone marrow suppression, numbness, allergic reactions, muscle pains, and diarrhoea. Other side effects include heart problems, increased risk of infection, and lung inflammation. Some concerns used during pregnancy may cause birth defects. Paclitaxel is in the taxane family of medications[1].

Paclitaxel disrupts microtubule function during cell division. Isolated from the Pacific yew in 1971, it was approved for medical use in 1993 and is included on the World Health Organization's List of Essential Medicines. It can be produced from precursors or through cell culture. Discovered through the US National Cancer Institute's screening of plants for anticancer properties, a crude extract from the bark of Taxus brevifolia was found to have cytotoxic activity against tumors in 1963. Paclitaxel was identified as the active component of this extract[2].

The development of paclitaxel faced challenges due to limited supply, leading to a shift toward semisynthetic production from 10-deacetylbaccatin III and other precursors found in more plentiful Taxus species like the European Yew (Taxus baccate). In 1979, its unique mechanism as an antitumor agent was discovered, showcasing significant efficacy in National Cancer Institute screenings. This exploration also resulted in docetaxel, which is derived from the same precursor and has slightly better water solubility and potency in acellular tubulin systems, though the clinical implications of these differences remain uncertain.

Chemistry of paclitaxel

Paclitaxel, a diterpenoid, is an important new anticancer drug first isolated from Western yew, *Taxus breuifolia*. The chemical name of paclitaxel is 5β,20- epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9- one-4,10-diacetate-2-benzoate 13 ester with (2*R*, 3*S*)-*N*-benzoyl-3-phenylisoserine (molecular for- mula $C_{47}H_{51}NO_{14}$; molecular weight 853.9). Paclitaxel differs structurally from other currently available antineoplastic agents (Kingston, 1991, Gregory and DeLisa, 1993).[4] Because of the complex and unusual chemistry of paclitaxel, it is mainly extracted from the bark

Paclitaxel is a white to off-white crystalline powder. It is highly lipophilic and practically insoluble in water. Although paclitaxel analogs appear to be another approach to overcome the problem of availability, the limiting factor is the construction of the taxane framework with its four-membered oxetane ring and a homochiral ester side-chain at C13, which becomes a challenge for synthetic chemists. Extensive studies have indicated that an intact taxane ring and an ester side-chain are essential for cytotoxic activity. In addition, it was shown that the presence of an accessible hydroxyl group at position 2″ of the ester side-chain enhances the cytotoxic activity of the drug. Modification of the side-chain has resulted in a more potent analog, docetaxel.

1962-68	NCI screening of cytotoxic agents from natural products
1967	Antitumor activity detected
1969	Pure paclitaxel isolated
1971	Structure elucidated
1983	Phase I studies initiated
1986	Hypersensitive reactions observed
1988	NCI suggests premedication regimen
1989	Proved effective against ovarian cancer
1991	Proved effective against breast cancer
1992	Proved effective against non-small cell lung cancer
1992	Approved by US FDA for ovarian cancer
1994	Approved by US FDA for breast cancer
	Total synthesis by Nicolaou and Holton, Independently
1994	Approved in India for ovarian cancer
1995	Approved in India for breast cancer

Fig 1: stages in the development of paclitaxel

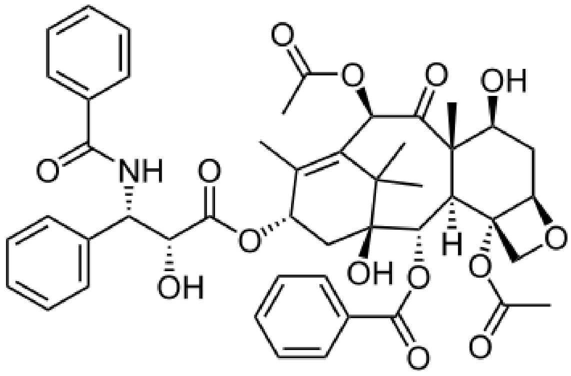

Fig 2 : chemical structure of paclitaxel

Mechanism of action:

Paclitaxel is one of several cytoskeletal drugs that target tubulin. Paclitaxel-treated cells have defects in mitotic spindle assembly, chromosome segregation, and cell division. Unlike other tubulin-targeting drugs, such as colchicine, that inhibit microtubule assembly, paclitaxel stabilizes the microtubule polymer and protects it from disassembly. Chromosomes are thus unable to achieve a metaphase spindle configuration. This blocks the progression of mitosis and prolonged activation of the mitotic checkpoint triggers apoptosis or reversion to the G0-phase of the cell cycle without cell division.

The ability of paclitaxel to inhibit spindle function is generally attributed to its suppression of microtubule dynamics, but other studies have demonstrated that suppression of dynamics occurs at concentrations lower than those needed to block mitosis. At the higher therapeutic concentrations, paclitaxel appears to suppress microtubule detachment from centrosomes, a process normally activated during mitosis. Paclitaxel binds to the beta-tubulin subunits of microtubules.

Complex of α, β tubulin subunits and paclitaxel. Paclitaxel is shown as a yellow stick.

Paclitaxel is a potent chemotherapeutic agent classified as a taxane. It exerts its anticancer effects by disrupting microtubule dynamics, essential components of the cell's cytoskeleton.

Microtubule Stabilization

Paclitaxel binds to the β-tubulin subunits of microtubules, promoting their polymerization and preventing depolymerization. This stabilization results in the formation of abnormal microtubule bundles, disrupting normal cellular functions.

Mitotic Arrest

By stabilizing microtubules, paclitaxel interferes with the dynamic reorganization required during cell division. This interference leads to mitotic arrest at the G2/M phase of the cell cycle, preventing proper chromosome segregation.

Induction of Apoptosis

Prolonged mitotic arrest activates cellular pathways that lead to programmed cell death (apoptosis). This is particularly effective in rapidly dividing cancer cells.

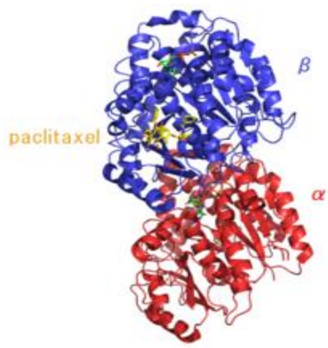

figure 3: α, β tubulin subunits and paclitaxel

Basic mechanism of the anti-cancer effect of paclitaxel

Paclitaxel belongs to the family of cytoskeletal drugs that target tubulin. As a result, paclitaxel treatment leads to abnormality of the mitotic spindle assembly, chromosome segregation, and consequently defects of cell division. By stabilizing the microtubule polymer and preventing microtubules from disassembly, paclitaxel arrests cell cycle in the G1/G2 and G /M phases and induces cell death in cancer. It has been known that inhibition of mitotic spindle using paclitaxel usually depends on its suppression of microtubule dynamics. However, recent studies demonstrated that only low-dose paclitaxel can do so, in contrast, high-dose paclitaxel might suppress microtubule detachment from the centrosomes. The binding site for paclitaxel has been identified to be the subunit of beta-tubulin. Paclitaxel has other mechanisms of action than for microtubule targeting. Panis etal found that the breast cancer patients after acute paclitaxel treatment exhibited immunosuppressive status by a strong type 2 helper T-cell (Th2) profile demonstrated by high levels of interleukin (IL)-10 and reported paclitaxel induced reactive oxygen species generation by enhancing the activity of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, which contributed to the potent anticancer activity of paclitaxel. The antineoplastic mechanisms of the non-chemotherapeutic use of paclitaxel were found. For example, reported that paclitaxel enhanced the efficacy of chemotherapy by blocking the immunosuppressive potential of myeloid-derived suppressor cells.

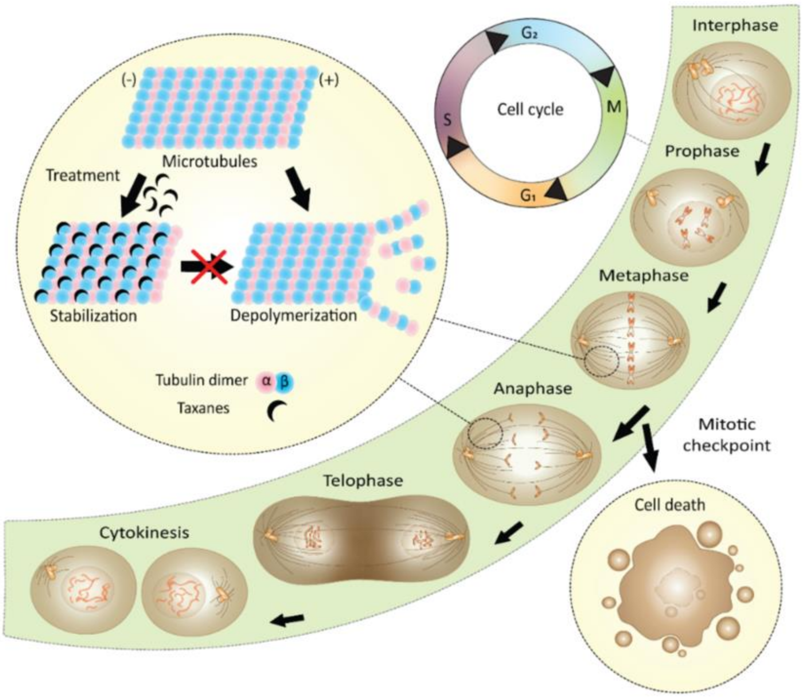

Fig 4: paclitaxel's effect on microtubules & mechanism of paclitaxel drug

Table 1: Physico-chemical properties

Parameter	Description
Molecular Formula	$C_{47}H_{51}NO_{14}$
Molar Mass	853.918 g·mol^{-1}
Appearance	white crystalline powder
Melting point	213–216°C
Solubility	ethanol, dimethyl sulfoxide (DMSO), and dimethyl formamide (DMF)
Drug type	Approved

Pharmacokinetic Profile of Paclitaxel

Paclitaxel is a widely used chemotherapeutic agent effective against various cancers, including ovarian, breast, and lung cancers. Its pharmacokinetic properties are influenced by factors such as formulation, dosing regimen, and patient-specific variables.

1. Formulations

- **Cremophor-diluted paclitaxel (Taxol®):** This formulation contains the solubilizing agent Cremophor EL, which can affect pharmacokinetics.
- **Nanoparticle albumin-bound paclitaxel (nab-paclitaxel, Abraxane®):** This formulation uses albumin nanoparticles to improve solubility and reduce hypersensitivity reactions.

2. Pharmacokinetic Parameters

- **Maximum Concentration (C_{max}):** Following a 3-hour infusion of 175 mg/m², the median C_{max} is approximately 5.1 µM, with an interquartile range of 4.5–5.7 µM.
- **Clearance (CL):** Total clearance is about 12.0 L/h/m², with an interquartile range of 10.9–12.9 L/h/m².
- **Time Above 0.05 µM (T>0.05 µM):** The median time paclitaxel concentration remains above 0.05 µM is 23.8 hours, with an interquartile range of 21.5–26.8 hours.

3. Infusion Duration and Nonlinearity

Paclitaxel exhibits nonlinear pharmacokinetics at higher doses and shorter infusion durations due to saturable processes in hepatic metabolism and distribution:

- **Short infusions (<6 hours):** Disproportionate increases in C_{max} and AUC with dose escalation
- **Prolonged infusions (>24 hours):** Tend to show more linear kinetics

This nonlinearity is also reported with nab-paclitaxel, though to a lesser extent due to formulation differences.

4. Interindividual Variability

Significant interindividual variability is observed in paclitaxel pharmacokinetics, influenced by factors such as body surface area, liver function, and genetic polymorphisms affecting drug metabolism and transport.Patient-specific factors such as hepatic enzyme activity (particularly CYP2C8 and CYP3A4), ABCB1 transporter polymorphisms, and liver function significantly affect paclitaxel pharmacokinetics. As a result, therapeutic drug monitoring and personalized dosing strategies are under investigation to improve treatment outcomes.

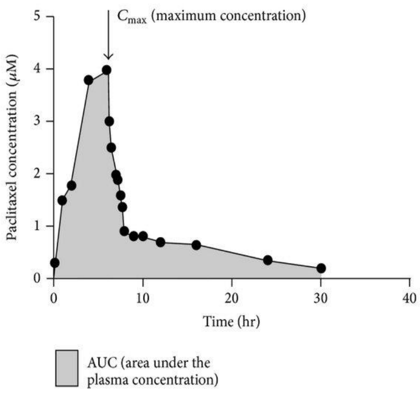

fig 5: AUC of paclitaxel

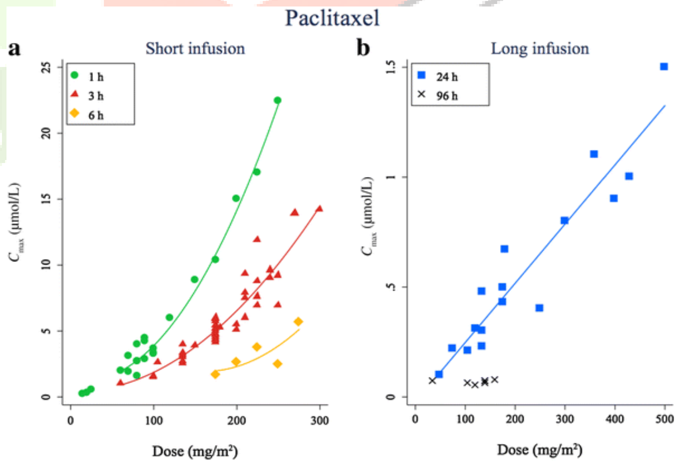

fig 6: pharmacokinetics of paclitaxel

Extraction Process of Paclitaxel

Paclitaxel, is primarily extracted from the bark of yew trees (*Taxus* species). The extraction and purification process involves several meticulous steps to ensure high purity and yield. The overview of the basic paclitaxel isolation and extraction scheme as follows.

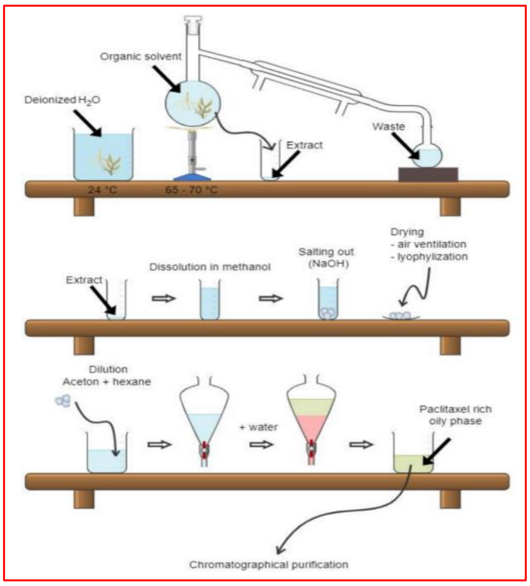

Fig 5: Paclitaxel is isolated from the bark, needles, or whole branches of yew.

Fig 6: Extraction of Paclitaxel

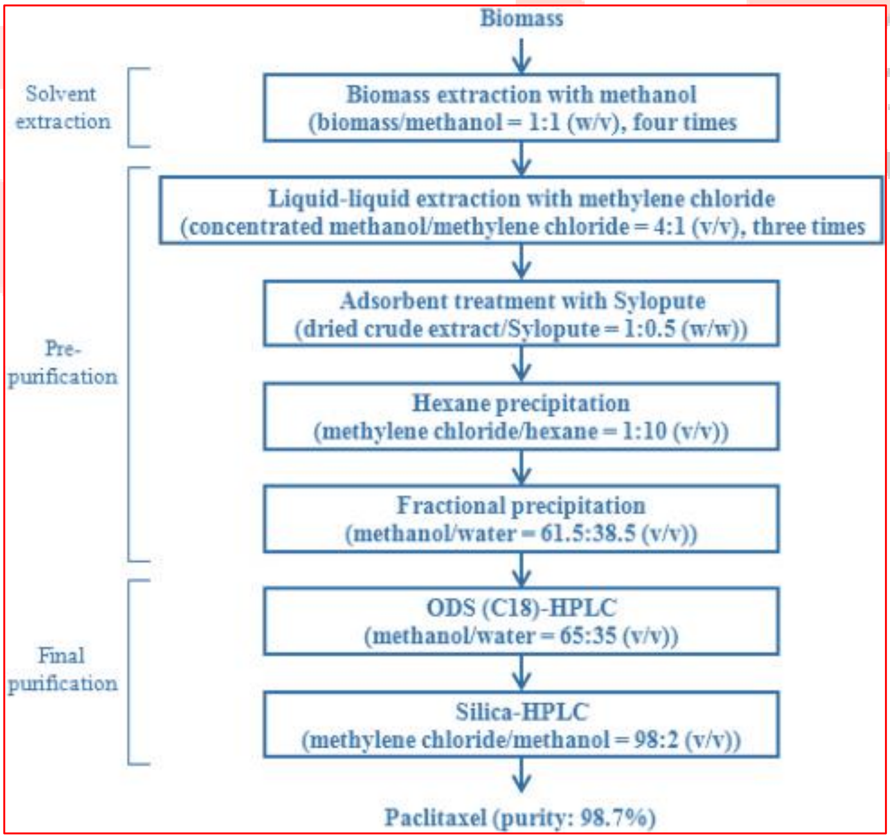

Fig 7: Scheme of basic paclitaxel isolation

Nanotechnology-Based Formulations of Paclitaxel

Nanotechnology has revolutionized drug delivery, offering innovative solutions to overcome the **limitations** of conventional paclitaxel formulations, such as **poor solubility, systemic toxicity, and resistance**. Below are some notable **nano formulations of paclitaxel**, highlighting their key features, benefits, and challenges.

1. Nanoparticle Albumin-Bound Paclitaxel (nab-paclitaxel, Abraxane®)

Composition: Nab-paclitaxel is a formulation of paclitaxel bound to human serum albumin nanoparticles, bypassing the need for toxic solvents like Cremophor EL.

Mechanism: The albumin component facilitates passive targeting to tumor cells via the **albumin receptor** (gp60) and **secreted protein acidic and rich in cysteine** (SPARC), which are often overexpressed in tumor vasculature.

Benefits:

- Improved solubility and reduced toxicity (no Cremophor EL).
- Enhanced tumor targeting and uptake.
- Better pharmacokinetics with reduced hypersensitivity reactions.

Clinical Use: Approved for the treatment of metastatic breast cancer, non-small cell lung cancer, and pancreatic cancer.

2. Polymeric Micelles for Paclitaxel Delivery

Composition: Polymeric micelles are nano-sized carriers made from amphiphilic block copolymers (e.g., polyethylene glycol (PEG)-polylactic acid (PLA)) that self-assemble in an aqueous environment.

Mechanism: The hydrophobic core of the micelles encapsulates paclitaxel, while the hydrophilic shell stabilizes the nanoparticles in circulation, preventing premature drug release.

Benefits:

- Enhanced solubility of paclitaxel.
- Prolonged circulation time and reduced systemic side effects.
- Capability for co-delivery of other anticancer agents or targeting ligands.

Challenges: Stability of the micelles in circulation and control over drug release rate.

3. Liposomal Paclitaxel (Caelyx®/Doxil®)

Composition: Liposomes are lipid bilayer vesicles that encapsulate paclitaxel, offering protection from degradation and controlling drug release.

Mechanism: Liposomes improve paclitaxel bioavailability and prolong circulation time due to their size and the PEGylation of the liposomal surface.

Benefits:

- Increased drug concentration at the tumor site via the **Enhanced Permeability and Retention (EPR) effect**.
- Reduced systemic toxicity and improved pharmacokinetics.

Clinical Use: Used for treating ovarian cancer, breast cancer, and Kaposi's sarcoma.

4. Nanocrystal Formulations of Paclitaxel

Composition: Paclitaxel nanocrystals are prepared by reducing paclitaxel to a nanoscale size (<100 nm), improving its solubility and dissolution rate.

Mechanism: The nanocrystals maintain the therapeutic properties of paclitaxel while enhancing its bioavailability.

Benefits:

- Improved solubility and bioavailability without the need for solubilizing agents.
- Potential for oral delivery, which is a significant advantage over intravenous formulations.

Challenges: Physical stability of the formulation and potential for aggregation.

5. Dendritic Polymer-Based Nanoparticles

Composition: Dendrimers are highly branched, nanoscale polymer structures that can be engineered to encapsulate paclitaxel in their core.

Mechanism: Dendritic nanoparticles provide controlled drug release and surface functionalization for targeted delivery to cancer cells.

Benefits:

- High drug-loading capacity.
- Surface modification to facilitate active targeting via ligands (e.g., folate receptors or antibodies).

Challenges: Potential for toxicity due to the complex nature of dendrimers, especially in vivo.

6. Paclitaxel-Loaded Nanostructured Lipid Carriers (NLCs)

Composition: NLCs consist of a solid lipid core combined with a liquid lipid phase, creating a matrix that can entrap paclitaxel.

Mechanism: NLCs improve the stability and solubility of paclitaxel, and the lipids provide a biocompatible delivery system.

Benefits:

- Enhanced bioavailability and sustained release of paclitaxel.
- Biodegradable and non-toxic carrier.

Challenges: Difficulty in scaling up for commercial production and ensuring reproducible release profiles.

7. Cyclodextrin-Based Nanoparticles

Composition: Cyclodextrins are cyclic oligosaccharides that can encapsulate hydrophobic drugs like paclitaxel in their central cavity.

Mechanism: Paclitaxel is encapsulated in the hydrophobic cavity of cyclodextrins, improving solubility and stability.

Benefits:

- Enhanced solubility and reduced toxicity.
- Potential for targeted drug delivery when combined with other nanoparticles or targeting ligands.

Challenges: Stability issues during formulation and potential for low drug loading.

8. Mesoporous Silica Nanoparticles (MSNs)

Composition: MSNs are porous, silica-based nanoparticles with a high surface area that can be loaded with paclitaxel and other chemotherapeutic agents.

Mechanism: The mesopores enable high drug-loading capacity, and the surface can be functionalized for targeted delivery.

Benefits:

- High surface area and controlled release profiles.
- Versatility in functionalizing the surface for specific tumor targeting.

Challenges: Biocompatibility and toxicity concerns regarding silica-based materials.

Table 2: Marketed formulations of Paclitaxel:

Brand Name	Formulation	Manufacturer	Indications	Administration Route
Taxol	Injectable solution	Bristol-Myers Squibb	Ovarian cancer, breast cancer, non-small cell lung cancer, Kaposi's sarcoma	Intravenous (IV)
Abraxane	Albumin-bound nanoparticles	Celgene (Bristol-Myers Squibb)	Breast cancer, pancreatic cancer, non-small cell lung cancer	Intravenous (IV)
Paxene	Injectable solution	Hospira (Pfizer)	Ovarian cancer, breast cancer, non-small cell lung cancer, Kaposi's sarcoma	Intravenous (IV)
Onxol	Injectable solution	Teva Pharmaceuticals	Ovarian cancer, breast cancer, non-small cell	Intravenous (IV)

			lung cancer, Kaposi's sarcoma	
Paclical	Injectable solution	Sun Pharmaceutical	Ovarian cancer, breast cancer, non-small cell lung cancer, Kaposi's sarcoma	Intravenous (IV)
Nanoxel	Polymeric micellar formulation	Dabur Pharma	Breast cancer, ovarian cancer, non-small cell lung cancer	Intravenous (IV)
Lipusu	Liposomal formulation	Luye Pharma	Ovarian cancer, breast cancer, non-small cell lung cancer	Intravenous (IV)
Genexol-PM	Polymeric micellar formulation	Samyang Biopharmaceuticals	Breast cancer, ovarian cancer, non-small cell lung cancer	Intravenous (IV)

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

HPLC is a widely used analytical technique for separating and quantifying components in mixtures across scientific disciplines. It operates on chromatographic principles, with a liquid sample passing through a column packed with a stationary phase, interacting with a mobile phase. The high pressure in HPLC allows for efficient separations. It includes a sample injection system, a high-pressure pump, a separation column, a detector, and a data analysis system. HPLC is versatile, analysing a range of compounds from small organics to large biomolecules. Different modes like reverse-phase, normal phase, ion-exchange, and size-exclusion chromatography provide flexibility. HPLC is vital in pharmaceutical quality control, environmental pollutant monitoring, and ensuring food safety. Its high sensitivity and precision make it indispensable in modern analytical laboratories, driving advancements in research and industry.

LIQUID CHROMATOGRAPHY- MASS SPECTROMETRY

LC-MS combines liquid chromatography's separation abilities with mass spectrometry's detection and characterization capabilities. Widely used in chemistry, biochemistry, pharmaceuticals, environmental science, and metabolomics, it excels in analysing complex mixtures with high sensitivity and selectivity. The process involves liquid chromatography separating components in a sample, and mass spectrometry detecting and analysing these based on mass-to-charge ratio. LC-MS is versatile, handling a broad range of compounds, from small organics to large biomolecules. Applied in drug development, environmental analysis, food safety testing, and clinical research, it provides detailed insights into complex sample compositions, playing a crucial role in modern analytical laboratories and contributing significantly to scientific advancements.

UV- VISIBLE SPECTROSCOPY:

UV-visible spectroscopy is a powerful analytical method used across scientific disciplines to study how a sample absorbs or reflects UV and visible light. It provides insights into the electronic structure of molecules and is valuable for analysing the concentration of absorbing species. This technique is based on the principle of molecular absorption at specific wavelengths, leading to electronic transitions. The UV range (200-400 nm) and visible range (400-700 nm) are key areas for these transitions, involving the movement of electrons to higher energy orbitals. A UV-visible spectrophotometer comprises a light source, a monochromator or prism for wavelength isolation, a sample holder, and a detector to measure transmitted or reflected light intensity. The resulting absorption spectrum serves as a unique fingerprint for the substance. UV-visible spectroscopy has diverse applications. In chemistry, it quantitatively analyzes substance concentration based on absorbance, while biochemists use it for studying biomolecules like proteins. Environmental scientists apply it to monitor water quality and detect pollutants. In pharmaceuticals, it aids in quality control, and in material science, it helps understand electronic properties.

Table 3. HPLC analysis performed with biological samples

Matrix	Detector	Column	Mobile Phase	Gradient		Retention time (min.)
				Time	B	
Rat plasma and brain tissue	MS/MS (876;308)	BDS hypersil C_8 (5 µm, 500 x 21 mm)	(A) 10 mM NH_4HCO_2 aqueous buffer with 0.1% formic acid (B) MeOH	0 min 1.5 min 1.8min	60% 60% 95%	< 3.5
Human and rat blood	UV (230)	Inertsil ODS-3 (5 µm, 150 x 4.6 mm)	(A) water (B) ACN	50% B		**11.2**
Plasma	UV (227)	Supelcosil LC- 18 (3 µm, 150 x 4.6 mm)	(A) 20mM phosphate buffer pH 3 (B) ACN	45% B		< 15
Tumor cells	MS (527.3)	Agilent Zorbax SB (5 µm, 150 x0.5 mm)	(A) 30:70 ACN: Water with 0.1% (w/v) formic acid (B) 90:10 ACN: Water with 0.1% (w/v) formic acid	0 min 2 min 8 min	30% 30% 100%	**7.78**
Human and dog plasma	MS (854; 509)	Zorbax C18 (5 µm, 50 x 2.1 mm)	(A) water, 0.1% acetic acid (B) ACN, 0.1% acetic acid	50%B		**2.9**
Mouse plasma and tissue containing liposome- loaded paclitaxel	MS (854; 286)	Phenomenex Luna C18 (5 µm, 50 x 2.1 mm)	(A) 0.1% acetic acid:ACN (70:30) (B) 0.1% acetic acid:ACN (10:90)	0 min 0.4 min 0.8 min 1.0 min 3.4 min	25% 100% 100% 25% 25%	~ 2

Beagle plasma	MS (854.4/286.0)	Capcell pak c18 (5 µm, 50 x 2 mm)	(A) 5 m M ammonium, 0.1% formic acid (B) ACN	0 min 2.5 min 2.51 min 2.55 min 3.21 min	20% 20% 50% 98% 98%	**1.24**
Human plasma	MS (854.0)	Hypersil C18 (5 µm, 100 x 2 mm)	0.1% acid formic (A) MeOH (B) water	0 min 7 min	30% 70%	**3.2**
Human plasma	MS (854; 569)	Phenomenex (4 µm, 100 x 3 mm)	(A) MeOH (B) 1% TFA/ammonium trifluoroacetate in H_2O, pH 7	Isocratic 30% B		**6.1**
Human plasma	MS (876.4; 308.1)	Zorbaxsb-C_{18} (3.5 µm, 50 x 2.1 mm)	(A) ACN (B) 0.05% formic acid	Isocratic 35% B		**4.18**
Human Plasma	MS (854)	Zorbax C_{18} (5 µm, 150 x 2.1 mm)	(A) MeOH (B) 10 mM NH_4OH	Isocratic – 9 min 30% B		**3.8**
Rat plasma	MS (854.2; 286.1)	Betabasic C_{18} (5 µm, 150 x 0.1 mm)	A) 0.1% formic acid Water B) ACN	Isocratic - 5 min 65% B		**3.23**
Human plasma	MS (876.2; 307.9)	BEH C_{18} (1.7 µm, 50 x 2.1 mm)	(A) MeOH (B) 0.1% formic acid	Isocratic – 2 min 25% B		**0.62**
Cell samples	MS (854; 569)	Zorbax C_{18} (3.5 µm, 150 x 0.5 mm)	(A) 10:90 ACN: H_2O, 2 mM ammonium acetate, pH 3.2 (formic acid) (B) 90:10 ACN: H_2O 2 mM ammonium acetate	0 min 3 min 15 min 17min	25% 25% 85% 98%	**13.5**
Rat plasma	MS (876.3; 307.9)	Hypersil C_{18} (5 µm, 200 x 4.6 mm)	(A) MeOH 0.1% formic acid	Isocratic - 6 min 20% B		**4**

Rat tissue	MS (876.3; 307.9)	Hypersil C_{18} (5 µm, 200 x 4.6 mm)	(A) MeOH 0.1% formic acid	Isocratic - 6 min 20% B		**~4**
Human/mouse plasma and brain tumor tissue	MS (854; 509)	Zorbax C_{18} (5 µm, 150 x 2.1 mm)	(A) MeOH 10 mM NH^{+}_{3}	Isocratic - 9 min 30% B		**6.4**
Human plasma	MS (854.4; 286.2)	Hypersil ODS (3 µm, 30 x 4.6 mm)	(A) ACN (B) 0.1% formic acid	Isoratic - 7 min 50% B		**2.8**
Rat plasma	MS (854.3; 286.2)	Atlantis C_{18} (5 µm, 100 x 2.1 mm)	(A) ACN (B) 10 mM ammonium formate	Isocratic - 7 min 25% B		**2**
Human plasma and oral fluid	MS (854.4; 509.3)	Merck Purospher-RP (3 µm, 55 x 2 mm)	(A) 2 mM acetic acid/0.2 mM ammonium acetate in water (B) 2 mM acetic acid/0.2 mM ammonium acetate in methanol	0 min 1.8 min 2 min 5 min	63% 73% 95% 95%	**3.2**
Mouse plasma and brain tissue	MS (854.3)	Hypersil (5 µm, 100 x 2.1 mm)	500 mL 0.1% formic acid 500 mL ACN	Isocratic - 8 min		**6.2**
Human plasma	MS (854.6; 286.2)	Zorbax (5 µm, 150 x 4.6)	(A) ACN (B) 2 mM ammonium acetate, pH 5	0 min 0.5 min 1 min 4.5 min	35% 35% 2%	**2%**
Dried blood	**MS (876; 569)**	**Oyster ODS3 (3 µm, 50 x 4.6 mm)**	(A) **Water** (B) **ACN**	**Isocratic - 7 min 60% B**		**~5**

Table 4. HPLC analysis performed with diverse matrices

Matrix	Detector	Column	Mobile Phase	Gradient		Retention Time (min.)
				Time	B	
Plant extract	MS (854.4; 286.1)	Eclipse XDB- C18, 5µm, 150 x 4.6mm	(A) Water (B) ACN	Isocratic - 36 min 60% B		31.56
Bulk drug and injectable dosage form	UV (200-400nm)	Whatman TAC- 1 5 µm, 250 x 4.6 mm	(A) Water (B) ACN	(A) Isocratic - 12 min 38% B Gradient 4%/min		17
Plant extract, body fluid and tissues	MS (854.2; 286.1)	Kinetex C_{18} 2.6 µm, 100 x 3 mm	(A) 0.1%HAc, NH_4Ac: MeOH (B) 90:10 (A): MeOH	0 min 1 min 6 min 11 min 13 min	5% 40% 65% 95% 95%	7.3
Copaiba essential oil extract	UV (228)	Uptisphere C- 18 3 µm, 150 x 3 mm	(A) Water (B) ACN	Isocratic - 15 min 50% B		~9.7
Plant extract	UV (227)	Eclipse XDB- C18, 5 µm, 250 x 4.6 mm	(A) 10 mM NH_4Ac (B) ACN	0 min 3 min 35 min 45 min 50 min	10% 10% 80% 95% 95%	36.8
Polymer	UV (227)	Inertsil ODS-3V (5 µm, 250 x4.6 mm)	(A) Water (B) ACN	0 min 15 min 23 min	50% 100% 100%	10.5
Formulations containing Cremophor EL	UV (227; 360)	Supelcosil LC-F (5 µm, 250 x4.6 mm)	(A) Water (B) ACN	20 min 60 min 70 min	70% 60% 60%	37.28

Keratin	MS (853.9)	Symmetry C_{18} (3.5 µm, 100 x2.1 mm)	(A) ACN (B) water, 0.1% formic acid	12 min 15 min 19 min	45% 100% 100%	9.1
Co-loaded paclitaxel liposome	UV (227)	Lichrospher C_{18} 5 µm, (250 x 4.6 mm)	(A) water (B) ACN	50% B		7.2
Paclitaxel in liposomal formulation	UV (227)	Lichrospher 100RP-18 (5 µm, 250 x 4.6mm)	(A) water (B) ACN	55% B		~ 6
Paclitaxel-loaded PEGylated immune liposome	UV (227)	Lichrospher 100 RP-18 (5 µm, 250 x 4.6 mm)	(A) water (B) ACN	50%B		6.8
Paclitaxel- dendrimer conjugate	UV (230)	Phenomenex C18 (5 µm, 250 x 4.6 mm)	(A) MeOH (B) 0.05% w/v TFA	20% B		6.2
Polymeric micelle	UV (227)	Bondapak-C18 (5 µm, 250 x3.9 mm)	(A) 0.01 M KH2PO4 (B) ACN, pH 3.5	65% B		7.4
Paclitaxel-loaded PLGA nanoparticles	UV (227)	Sunfire Water (5 µm, 250 x 4.6 mm)	(A) Water (B) ACN	60% B		5.6
PEGylated liposomal paclitaxel	UV (227)	Lichrosphere RP-18 (5 µm, 250 x 4.6 mm)	(A) water (B)ACN	50% B		6.2
Paclitaxel-loaded nanoparticles	UV (228)	Phenomenex (5 µm, 250 x 3.2 mm)	(A) Ammonium acetate 10 Mm (B) ACN	45% B		7.1

Conclusion:

The development of nanoparticle formulations for paclitaxel has significantly enhanced its therapeutic efficacy and reduced side effects compared to conventional formulations. These innovative nano-based systems offer targeted delivery, improved solubility, and sustained release, paving the way for personalized cancer treatments. However, challenges related to stability, scalability, and biocompatibility still need to be addressed for broader clinical applications. Paclitaxel remains a cornerstone in cancer therapy, renowned for its unique mechanism of action and remarkable efficacy against a wide range of malignancies. Its complex chemical structure, coupled with its distinctive physicochemical properties, presents both challenges and opportunities for pharmaceutical development and analytical characterization. Over the years, advancements in analytical methods, including HPLC, LC-MS, and spectroscopic techniques, have significantly enhanced the precision and reliability of paclitaxel quantification, quality control, and pharmacokinetic studies. Despite its success, challenges such as drug resistance, limited solubility, and sourcing issues persist, driving ongoing research into novel formulations, synthetic pathways, and targeted delivery systems. As scientific understanding deepens and technology evolves, paclitaxel continues to inspire innovation in oncology and beyond, promising a brighter future for cancer treatment and therapeutic applications. This review covers the different analytical methods for its quantification and underscores the importance of continued exploration and optimization to fully harness the potential of this extraordinary compound.

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