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ADVERSE DRUG REACTIONS AND DRUG INTERACTIONS OF TAXANES

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ABSTRACT

Paclitaxel and docetaxel are key chemotherapy agents for various cancers, but their use is often limited by adverse drug reactions (ADRs) and drug–drug interactions. A review of clinical and pharmacokinetic studies was performed to identify major ADRs and interaction mechanisms. Adverse drug reactions of taxanes frequently include neutropenia, peripheral neuropathy (worsened by cumulative dosing), hypersensitivity (linked to solvents Cremophor EL and polysorbate 80), alopecia, mucositis, and GI upset. Both drugs are metabolised by CYP3A4 and CYP2C8. CYP inhibitors can raise toxicity risk; inducers may reduce efficacy. The timing of taxanes with agents like cisplatin or anthracyclines also impacts toxicity and effectiveness. Effective use of taxanes requires vigilant monitoring, personalised dosing, premedication, and awareness of interactions. These strategies help maximise efficacy and minimise harm.

KEYWORDS: Taxanes, Paclitaxel, Docetaxel, Nab-paclitaxel, Adverse drug reactions, Drug interactions.

INTRODUCTION

Phytochemicals—natural compounds from plants—have been widely studied for their ability to help prevent and treat many human diseases, mainly because they come from nature and have various biological effects. Among these, plant-derived alkaloids have garnered considerable attention for their potent therapeutic properties, especially their cytotoxic effects against cancer cells.

One particularly notable class of plant alkaloids is **taxanes, a group of diterpenoid compounds recognised** for their powerful antineoplastic (anti-cancer) activity. The discovery and development of taxanes mark a pivotal advancement

in the field of oncology, significantly influencing the way many cancers are treated today. These compounds exert their effects primarily by stabilising microtubules, disrupting cell division, and promoting apoptosis in cancer cells.

What sets taxanes apart from many other chemotherapeutic agents is their broad spectrum of efficacy across various malignancies. They have been successfully incorporated into treatment protocols for cancers such as breast, ovarian, lung, and prostate cancer, among others. As a result, taxanes have become an integral part of modern chemotherapy regimens and are often used in combination with other agents to enhance therapeutic outcomes.

The most widely used taxane-based chemotherapeutic drugs in clinical settings include **paclitaxel**, **docetaxel**, and the semi-synthetic derivative **cabazitaxel**. These agents have been extensively studied and have demonstrated both efficacy and tolerability in numerous clinical trials, solidifying their role as cornerstone therapies in cancer management.

The yew tree, a member of the **Taxaceae** family, is a distinctive and ancient evergreen gymnosperm notable for its absence of cones and resin—traits that set it apart from many other conifers. There are approximately 24 recognised species of yew, all characterised by slow growth and the potential to reach impressive dimensions—up to 30 m in height and 5 m in trunk diameter.

Despite its botanical elegance, the yew is notoriously toxic. Throughout history, its poisonous nature has been exploited for various fatal purposes, including suicides, deliberate poisonings, and even as a means of enhancing the lethality of weapons.

The **importance of the yew tree grew a lot when paclitaxel, a strong cancer-fighting drug first found in the bark of the Pacific yew (Taxus brevifolia), was discovered.** However, the extraction of paclitaxel posed a major challenge due to the limited availability of the Pacific yew and the need for large quantities of bark, which threatened sustainability and ecological balance.

This scarcity prompted researchers to identify alternative and more sustainable sources. The **European yew** (*Taxus baccata*), being more readily available, emerged as a primary substitute for paclitaxel production. Additionally, other species like the **Canadian yew** (*Taxus canadensis*) and the **Chinese yew** (*Taxus chinensis*) have been explored for their potential to yield taxane compounds. In India, the **Himalayan yew** (*Taxus wallichiana*) serves as the indigenous source of taxanes.

To date, scientific investigations have led to the identification of **over 400 taxane diterpenoids** across various species of the *Taxus* genus. These valuable compounds have been extracted from multiple parts of the tree—including the bark, leaves, and seeds—highlighting the genus as a rich and diverse source of pharmacologically active molecules.[1]

Mechanism of action of taxanes

Microtubules are flexible structures made of tubulin proteins that are important for maintaining cell shape, helping transport materials inside the cell, and managing cell division. Taxanes interfere with microtubule function by excessively stabilising these structures, thereby inhibiting their natural ability to assemble and disassemble. This disruption hampers the proper progression of mitosis, preventing cancer cells from dividing and proliferating. Consequently, the affected cells become arrested in the cell cycle and are ultimately driven to programmed cell death, or apoptosis.[1]

Although paclitaxel and docetaxel—both members of the taxane family—share structural similarities, they exhibit distinct pharmacological properties. Each drug targets a beta subunit of tubulin, thereby influencing microtubule polymerisation. However, their effects on the cell cycle differ. Paclitaxel mainly stops cells from moving from the G2 phase to the M phase of the cell cycle, while docetaxel is better at causing cell death during the S phase, when DNA is being made.[2]

Paclitaxel: Paclitaxel is a landmark anticancer agent originally isolated from the bark of the Pacific yew tree (*Taxus brevifolia*). Its discovery represented a major breakthrough in cancer therapy and led to its approval by the U.S. Food and Drug Administration (FDA) in 1992 for the treatment of ovarian cancer. Building on this success, the FDA approved its use for breast cancer in 1994, establishing paclitaxel as a key component of modern chemotherapy regimens.

Despite its effectiveness, paclitaxel presents formulation challenges due to its strong lipophilic properties, which make it nearly insoluble in water. To get around this problem, the drug is given in a mixture that is half Cremophor EL (a type of castor oil) and half dehydrated alcohol. However, Cremophor EL is known to cause hypersensitive reactions in some patients, necessitating pre-treatment with corticosteroids and antihistamines to minimise the risk of adverse effects.[3]

Docetaxel: Docetaxel is a semi-synthetic derivative of paclitaxel, first identified for its anticancer properties in 1991. It is produced from the needles of the European yew (*Taxus baccata*), using a precursor compound known as 10-deacetyl baccatin III. Docetaxel is different from paclitaxel because it has a hydroxyl group at the 10th carbon and a tert-butyl carbamate ester attached to its side chain.

Like paclitaxel, docetaxel is highly lipophilic and poorly soluble in water, but it can be dissolved in organic solvents such as ethanol, methanol, and chloroform. Its clinical formulation employs 100% polysorbate 80 as a solubilizing agent. In laboratory studies, docetaxel has demonstrated 2–3 times greater potency than paclitaxel in inducing tubulin polymerisation, along with a higher binding affinity for its target.[4]

Cabazitaxel: Cabazitaxel is a semi-synthetic taxane derived from 10-deacetyl-baccatin III. While it has a similar basic structure to docetaxel, it is different because it has two methoxy groups instead of hydroxyl groups on its side chain. Like other taxanes, cabazitaxel is highly lipophilic and poorly soluble in water, but it can be dissolved in ethanol. Its pharmaceutical formulation, similar to that of docetaxel, employs polysorbate 80 as a solubilizing agent.

While both paclitaxel and docetaxel have been approved for the treatment of a wide range of cancers, cabazitaxel has been specifically approved for use in patients with castration-resistant prostate cancer, offering a treatment option when other therapies have failed.

Nanoparticle-albumin-bound paclitaxel (Nab-paclitaxel): Nab-paclitaxel is a form of paclitaxel that is attached to albumin and made into tiny particles that are about 130 nanometers in size. This design improves permeability and retention within tumours, facilitating the passive targeting of cancer cells. Nab-paclitaxel does not contain solvents like traditional paclitaxel formulations, so patients do not need to take corticosteroids or antihistamines beforehand to avoid allergic reactions.

The recommended dosing regimen includes 260 mg/m² administered intravenously over 30 minutes every three weeks or 100–125 mg/m² on days 1, 8, and 15 in a 28-day treatment cycle. After reconstitution, the formulation remains chemically stable for up to 8 hours.

Pharmacokinetically, nab-paclitaxel demonstrates linear behaviour, which leads to more consistent tumour distribution and a predictable dose-response relationship, in contrast to the nonlinear kinetics of conventional paclitaxel. In a U.S. clinical study comparing the two, nab-paclitaxel was associated with fewer adverse effects, including reduced rates of anaemia, diarrhoea, neuropathy, and pain, along with a decreased reliance on antiemetics, antihistamines, and steroids. The incidence of hypersensitivity reactions is very low, reported at under 1%.

Although treatment outcomes vary across different studies, nab-paclitaxel demonstrated promising results specifically in pancreatic adenocarcinoma, which is a type of cancer where conventional paclitaxel had limited efficacy. This success led to FDA approval in 2013 for use in combination with gemcitabine for pancreatic cancer. Additionally, nab-paclitaxel is approved for treating metastatic breast cancer and non-small cell lung cancer (NSCLC).[1]

Metabolism of Taxanes

Taxanes are mainly broken down in the liver, where they are changed by cytochrome P-450 enzymes and then removed from the body through bile. The specific enzymes involved in their metabolism differ between compounds: **CYP2C8** is mainly responsible for the hydroxylation of **paclitaxel**, while **CYP3A4** plays a key role in metabolising **docetaxel**.[2]

ADVERSE DRUG REACTIONS OF TAXANES

Hematologic toxicity: Hematologic toxicity, especially neutropenia, is a common side effect of taxane therapy, with its frequency varying by drug. Paclitaxel generally causes less hematologic toxicity than docetaxel.[41] Neutropenia can escalate to febrile neutropenia, a serious condition that may require hospitalisation and antibiotic treatment. This complication is more frequently associated with docetaxel, often leading to the preventive use of antibiotics. Taxanes can also cause anaemia, thrombocytopenia, and leukopenia, increasing the risk of fatigue, infections, and bleeding. Management typically includes supportive treatments such as blood transfusions, growth factors, and antibiotics.[5]

Neurotoxicity: Taxane therapy—especially with paclitaxel—often comes with a well-known downside: nerve damage. The most common issue is **painful peripheral neuropathy**, where patients feel tingling, numbness, or burning in their hands and feet. This symptom is so frequent and severe that it often becomes the main reason doctors reduce or stop the treatment. But that's not all. **Researchers are increasingly linking these drugs to effects on the central nervous system.** Patients may experience **cognitive difficulties**, such as trouble remembering, focusing, or processing information, and in rare cases, **encephalopathy**—a serious condition involving confusion or changes in consciousness.[6] Common symptoms include burning sensations, numbness, tingling, and sharp pains that typically occur in a glove-and-stocking distribution. Motor neuropathy is rare and usually mild, with minimal interference in daily function. The overall effect of neurotoxicity on quality of life remains underexplored, highlighting the need for a thorough evaluation using standardised assessment tools.[7]

Gastrointestinal toxicity: A common adverse reaction to taxane-based chemotherapy is gastrointestinal discomfort—with symptoms like nausea, vomiting, diarrhoea, and constipation—which appears at different rates in different populations. For example, research indicates that Tunisian patients receiving taxane treatment experience much higher

levels of digestive and nail problems but have noticeably fewer blood-related side effects compared to other groups.[8] When multiple chemotherapeutic agents offer similar effectiveness in advanced cancers, the side effect profile and impact on quality of life become key factors in treatment decisions. Although paclitaxel and docetaxel show comparable efficacy, their toxicity profiles differ. Gastrointestinal side effects—such as nausea, vomiting, diarrhoea, and constipation—are frequently associated with taxane treatment.[9]

Dermatological toxicities

- **Immediate hypersensitivity reactions:** Hypersensitivity reactions to taxanes—both paclitaxel and docetaxel—typically occur during or shortly after infusion, often within minutes of initiation. Without premedication, such reactions can affect around **30–40%** of patients, though this drops to **1–2%** with proper steroid and antihistamine pretreatment. Manifestations range in severity from urticaria, flushing, pruritus, and angioedema to systemic symptoms like hypotension, bronchospasm, dyspnea, chills, and back pain.[11]
- **Extravasation reactions**: The extravasation (leakage) of chemotherapy into surrounding soft tissues occurs in about **0.1%–6%** of patients. Specifically, **when paclitaxel is given through a 24-hour infusion, about 1.6% of patients experience problems at the injection site, including leakage, while docetaxel causes these issues in less than 1% of patients.** Most reactions are mild irritant responses, but severe extravasations from both agents can occasionally lead to serious complications such as tissue necrosis or chronic ulceration.[12]
- **Photosensitivity:** Both paclitaxel and docetaxel can trigger inflammatory rashes—predominantly in sun-exposed areas (phototoxic reactions)—though overall incidence in breast cancer patients is under 1%. This photosensitivity occasionally manifests as photo-distributed erythema multiforme, and it is thought to be induced by taxane-driven disruptions in porphyrin synthesis, especially under UVB exposure.[13]
- **Nail changes:** Taxane chemotherapy commonly causes a wide range of nail abnormalities. These can stem from damage to the nail matrix—leading to melanonychia, true leukonychia, Beau's lines, onychomadesis, brittleness with ridging and thinning, onychorrhexis, and koilonychia—or from effects on the nail bed, causing onycholysis and apparent leukonychia.[14] Taxane-induced nail lesions typically become apparent several weeks into treatment due to the slow growth of the nail plate, and their prevalence intensifies with increased treatment cycles. These changes are more frequently observed with weekly taxane regimens, though they also occur in those administered every three weeks.[15]

Alopecia:— Paclitaxel and docetaxel are among the most well-known chemotherapeutic agents that frequently lead to alopecia, primarily through a process known as dystrophic anagen effluvium. Hair loss generally begins after the initial treatment cycle, regardless of whether the drugs are used in adjuvant or metastatic settings, and typically involves widespread scalp thinning in at least 60% of patients. **Chemotherapy doesn't just affect the hair on your head—it can cause hair loss in many other places, too.**

Eyelashes and eyebrows may thin or fall out, and you might notice changes in your beard, underarms, pubic area, and even body hair. This type of loss is more likely to happen if you're on longer treatment plans, higher drug doses, or going through several chemo cycles. Chemo targets fast-growing cells—cancer cells—but unfortunately, hair follicles are also fast-growing. So, the drugs can't tell the difference, leading to the thinning or shedding of hair in many areas, not just the scalp. Most people start noticing hair loss about 1–3 weeks into treatment, and it may continue gradually or all at once as you go through more chemo cycles.

Hair regrowth commonly begins within 3 to 6 months following the completion of therapy and generally progresses back to the patient's original hair volume and coverage. However, more than one-third of individuals report that their new hair grows back with noticeable changes, often being curlier in texture and different in colour—most commonly greyer, though darkening may also occur in some cases.[16,17]

Pneumonitis: Docetaxel has been associated with cases of drug-induced pneumonitis, most frequently manifesting as interstitial pneumonitis in patients undergoing treatment for different types of cancer. While this adverse effect is considered uncommon, occurring in approximately 4.6% of individuals receiving the standard three-weekly regimen, it can pose a significant clinical concern due to its potential severity.[18]

DRUG INTERACTIONS OF TAXANES

Drug interactions with taxanes, like paclitaxel and docetaxel, are important to think about, especially when they are used with other chemotherapy drugs. Because both taxanes are broken down in the liver mainly by the cytochrome P450 (CYP) enzyme system, any other drugs taken at the same time that affect these processes can greatly change how the taxanes are absorbed, distributed, metabolised, and eliminated from the body.

Taxanes are specifically metabolised by CYP3A and CYP2C isoenzymes. So, if there are other drugs that increase or decrease the activity of these enzymes, it can change how quickly paclitaxel and docetaxel are removed from the body and how much of the drug is in the blood, which could lead to more side effects or make the treatment less effective.
Several specific examples illustrate the complexity of these interactions:

- **Paclitaxel and Cisplatin**: Giving paclitaxel before cisplatin reduces its clearance, leading to an increase in drug exposure. Interestingly, cisplatin does not stop the breakdown of paclitaxel in isolated liver microsomes, which means the interaction isn't caused by direct interference in how the body processes the drug. Instead, pharmacodynamic interactions are likely involved. For example, higher amounts of DNA adduct in white blood cells suggest that cisplatin may work together with both paclitaxel and docetaxel in a way that influences how well the treatment works and its side effects.
- When paclitaxel is given with carboplatin, there are no significant changes in how the body processes these drugs, so their levels and breakdown stay the same. However, from a pharmacodynamic perspective, the combination leads to reduced thrombocytopenia (low platelet count) compared to carboplatin alone. This finding suggests a protective or modulating effect of paclitaxel on bone marrow suppression when used with carboplatin, although the exact mechanism is not fully understood.
- **Paclitaxel or Docetaxel with Alkylating Agents**: The sequence of administration significantly impacts toxicity profiles. For instance, giving paclitaxel before cyclophosphamide results in enhanced myelosuppression, indicating increased bone marrow toxicity. On the other hand, when docetaxel is administered prior to ifosfamide, a commonly used alkylating agent, the observed toxicity appears to be less severe. Although the exact biological pathways behind these interactions remain unclear, the findings underscore the importance of drug sequencing in minimising adverse effects.
- Combination treatments with paclitaxel and doxorubicin show that when and how drugs are given can create complicated interactions in how the body processes and responds to them. For example, co-administration can affect drug distribution and clearance rates, as well as amplify toxicity or therapeutic response. These interactions

might happen because the drugs share similar ways of being processed in the body, compete for the same proteins, or work together at the molecular level to impact DNA damage or cell death in tumour cells.

The way taxanes work with other chemotherapy drugs isn't just about changes in how the body processes them; it often includes complex mechanisms that impact how well they work and their safety. Understanding these interactions necessitates careful consideration of the following factors:

- Drug metabolism pathways
- Enzyme inhibition or induction
- Order and timing of administration
- Molecular-level synergies or antagonisms

So, when creating effective treatment plans that include taxanes, it's important to use proven methods for the order of medications and to carefully monitor the patient to achieve the best tumour control while keeping side effects low.[19]

INHIBITORS AND INDUCERS OF CYTOCHROME ENZYMES[20]

CYP2C8 INHIBITORS

- Gemfibrozil
- Clopidogrel
- Montelukast
- Zafirlukast
- Clotrimazole
- Felodipine
- Mometasone furoate

CYP2C8 INDUCERS

- Rifampicin
- Carbamazepine
- Phenobarbital
- St. John's Wort
- Griseofulvin
- Phenytoin

CYP3A4 INHIBITORS

- **Antifungals**: Ketoconazole, itraconazole.
- **Antibiotics**: Erythromycin, clarithromycin.
- **Antiretrovirals**: Ritonavir.
- **Calcium Channel Blockers**: Verapamil, diltiazem.
- **Antidepressants**: Many SSRIs and SNRIs, such as fluoxetine, fluvoxamine, and others.
- **Other**: Grapefruit juice

CYP3A4 INDUCERS

- Phenobarbital
- Phenytoin
- Rifampin.
- St. John's Wort
- Glucocorticoids
- Other examples include:

Carbamazepine, efavirenz, and certain statins (e.g., simvastatin)

Table 2: CYP3A4 Inhibitors and Inducers

CONCLUSION

Taxanes, such as paclitaxel and docetaxel, are commonly utilised chemotherapy drugs that are vital in treating various types of cancer. Despite their effectiveness, notable adverse drug reactions (ADRs) and the risk of drug interactions frequently challenge their use.

Common side effects of taxane therapy include reduced bone marrow function (especially low white blood cell counts), nerve damage, allergic reactions, hair loss, inflammation of the mucous membranes, and stomach problems. These adverse effects can greatly impact a patient's quality of life and may require dose adjustments or even stopping the treatment. Prolonged use often worsens neuropathy.

Taxanes are extensively metabolised in the liver, mainly through cytochrome P450 enzymes—particularly CYP3A4 and CYP2C8. When taken with drugs that affect these enzymes, the amount of taxanes in the blood can change, which might lead to more side effects or less effectiveness. Additionally, the timing and sequence of administering taxanes with other cancer drugs can influence treatment effectiveness due to pharmacodynamic interactions.

In summary, while taxanes are potent anticancer agents, vigilant monitoring of side effects and drug interactions is crucial. Tailoring doses to individual patients, using appropriate premedications, and considering patient-specific risk factors are key to maximising benefits and minimising risks during taxane chemotherapy.

REFERENCES

1. Jose WM. Taxanes—the backbone of medical oncology. Indian J Med Paediatr Oncol, 2020; 41: 221-34.
2. Dorr RT. Pharmacology of the taxanes. Pharmacotherapy, 1997 Sep-Oct; 17(5 Pt 2): 96S-104S. PMID: 9322876.
3. Ma P, Mumper RJ. Paclitaxel nano-delivery systems: A comprehensive review. J Nanomed Nanotechnol, 2013; 4: 1000164.
4. Buey RM, Barasoain I, Jackson E, Meyer A, Giannakakou P, Paterson I, et al. Microtubule interactions with chemically diverse stabilising agents: the thermodynamics of binding to the paclitaxel site predicts cytotoxicity. Chem Biol, 2005; 12: 1269-79.
5. Markman M: Management of toxicities associated with the administration of taxanes. Expert Opin Drug Saf, 2003; 2: 141-6. 10.1517/14740338.2.2.141.
6. da Costa R, Passos GF, Quintão NL, Fernandes ES, Maia JR, Campos MM, Calixto JB: Taxane-induced neurotoxicity: pathophysiology and therapeutic perspectives. Br J Pharmacol, 2020; 177: 3127-46. 10.1111/bph.15086.

7. Kuroi K, Shimozuma K: Neurotoxicity of taxanes: symptoms and quality of life assessment. Breast Cancer, 2004l; 11: 92-9. 10.1007/BF02968010.
8. Ben Nasr S, Zribi A, Ben Hassen M, and colleagues conducted a retrospective study involving 90 Tunisian cancer patients to assess the toxicity profile of taxanes. Bull Cancer, 2021; 108: 266-71. 10.1016/j.bulcan.2020.10.018.
9. Guastalla JP 3rd, Diéras V: The taxanes: toxicity and quality of life considerations in advanced ovarian cancer. Br J Cancer. 2003; 89 Suppl 3: S16-22. 10.1038/sj.bjc.6601496.
10. Caiado J, Picard M. Tests to check for allergic reactions to platinum drugs and taxanes include skin tests, specific IgE, and substances released by mast cells and basophils. Curr Allergy Asthma Rep, 2014; 14:451. [PubMed: 24951237].
11. Lee C, Gianos M, and Klaustermeyer WB conducted a study on the diagnosis and management of hypersensitivity reactions associated with common cancer chemotherapy agents. Ann Allergy Asthma Immunol, 2009; 102: 179-87. [PubMed: 19354063].
12. Barbee MS, Owonikoko TK, Harvey RD. Taxanes: vesicants, irritants, or just irritating? Ther Adv Med Oncol, 2014; 6: 16–20. [PubMed: 24381657].
13. Tokunaga M, Iga N, Endo Y, et al. reported elevated protoporphyrin levels in patients with skin cancer who were receiving taxane chemotherapy. Eur J Dermatol, 2013; 23: 826–9. [PubMed: 24480579].
14. Gilbar P., Hain A., and Peereboom VM. The article titled "Nail toxicity induced by cancer chemotherapy" was published in the Journal of Oncology Pharmacy Practice, 2009; 15: 143–155 in. [PubMed: 19171552].
15. Winther D, Saunte DM, Knap M, et al. Nail changes due to docetaxel—a neglected side effect and nuisance for the patient. Support Care Cancer, 2007; 15: 1191–7. [PubMed: 17318589].
16. Trueb RM discusses whether chemotherapy-induced anagen effluvium presents as diffuse or patterned. Dermatology. 2007; 215: 1–2. [PubMed: 17587831].
17. Paus R, Haslam IS, Sharov AA, and others contributed to this study. The study delves into the pathobiology of hair loss caused by chemotherapy. Lancet Oncol, 2013; 14: e50–9. [PubMed: 23369683].
18. Tamiya A, Naito T, Miura S, Morii S, Tsuya A, Nakamura Y, et al. Docetaxel is linked to interstitial lung disease in patients suffering from advanced non-small cell lung cancer. Anticancer Res (2012) 32(3):1103–6.
19. Baker, S.D. Drug Interactions with the Taxanes. Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy, 1997; 17: 126S-132S. https://doi.org/10.1002/j.1875-9114.1997.tb03814.x.
20. The study was conducted by Filppula, Anne M., and her team. "Autoinhibition of CYP3A4 means that CYP2C8 plays a key role in how imatinib is broken down, and differences in CYP2C8 activity could change the levels of the drug in the blood and how well it works." Drug Metabolism and Disposition, *2013; 41(1): 50-59.*