INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Case Study Article

Cisplatin Induced Oral Mucositis - A Case Report

Reyaz Golsangi*[1], Samreen[2], Asha Raj[3], Vedant Bhoskar[4], Mohd Shahnawaz[5], Shaik Umair[6], Sayed Omer Ahmed[7]

[1]*Ramaiah Medical College Teaching Hospital.*
[2,3,4,5,6,7]*Jawaharlal Nehru Technological University Hyderabad.*

ARTICLE INFO

Published: 30 April. 2025
Keywords:
Oral mucositis, chemotherapy-induced mucositis, cancer therapy, adverse effects, supportive care, chemotherapy complications, case report, laryngeal cancer, CAP protocol, mucosal ulceration, pain management, inflammation, chemotherapy modifications.
DOI:
10.5281/zenodo.15310395

ABSTRACT

Oral mucositis (OM) is a serious side effect that often occurs in cancer patients undergoing chemotherapy and radiation treatment. The oral mucosa may develop red, painful, and ulcerative lesions, which can stop cancer therapy and greatly reduce the quality of life for patients. This study aims to emphasize the etiology, clinical presentation, and management strategies for chemotherapy-induced OM, illustrated through a case involving a 60-year-old male patient diagnosed with laryngeal cancer. The patient was receiving the CAP chemotherapy protocol, which includes cisplatin, doxorubicin, and 5-fluorouracil. After the third chemotherapy cycle, the patient developed Grade 3 OM, characterized by a swollen, erythematous patch localized to the tonsillar fossa, associated with severe pain and difficulty in swallowing. Management involved the administration of intravenous granisetron, dexamethasone, and pantoprazole, along with appropriate supportive care to prevent further complications and improve patient comfort. Nutritional support and oral hygiene measures were also incorporated into the care plan. In order to decrease patient morbidity and prevent treatment delays, the example emphasizes the need of early detection and prompt action in OM management. Effective management requires a combination of symptom relief, inflammation control, and, when necessary, chemotherapy dose adjustments. Prompt and multidisciplinary supportive care can enhance patient tolerance to ongoing cancer therapy, minimize hospitalizations, and improve overall outcomes. Recognizing OM as a potentially dose-limiting toxicity underlines the need for vigilant monitoring in patients undergoing intensive chemotherapy regimens.

INTRODUCTION

The reddening, swelling, and eventually ulceration of the mouth's mucosa that can develop in cancer patients undergoing radiation and chemotherapy is

***Corresponding Author:** Reyaz Golsangi
Address: Ramaiah Medical College Teaching Hospital.
Email ✉: riyazrj5557@gmail.com
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

called "oral mucositis" (OM). Criterion for Common Terminology of Adverse Events (CTCAE) was published by the National Cancer Institute (NCI). The subjective and objective assessments of mucositis are distinct. [1]

"Subjective	Objective
Grade 1	Mucosal erythema
Grade 2	Patchy ulcers or pseudomembranes
Grade 3	Confluent ulcers or pseudomembranes, minimal trauma-induced hemorrhage.
Grade 4:	tissue necrosis, substantial spontaneous bleeding, life-threatening implications
Grade 5	Death.

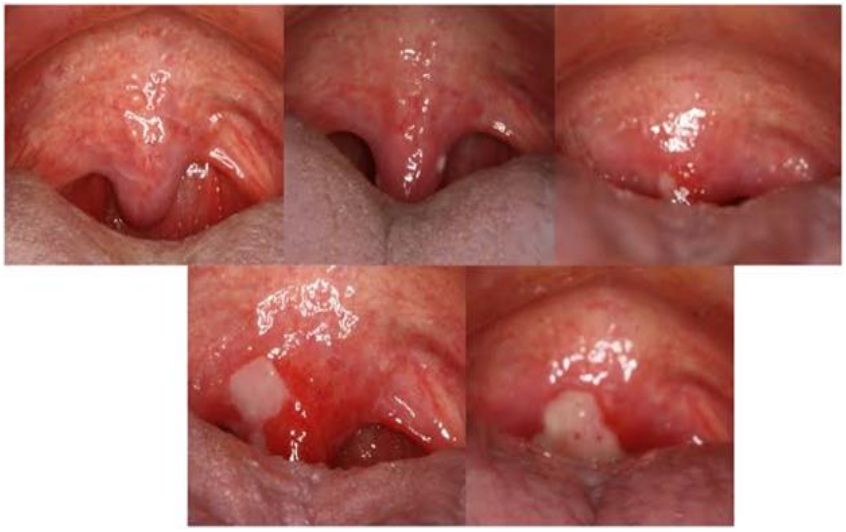
Etiology"

Patients receiving high-dose myeloablative chemotherapy for solid tumors or lymphomas, or hematopoietic cell transplantation, are at increased risk of developing oral mucositis. Oral mucositis is more common in some chemotherapy medications and less common in others. [2]

- Oral mucositis is common among chemotherapeutic medications that affect DNA synthesis (S-phase), including cytarabine, 5-fluorouracil, and methotrexate.
- Oral mucositis is more likely to occur in patients on anthracyclines, mTOR inhibitors, alkylating medications, or antimetabolites.

Impact Of Oral Mucositis

- Discomfort and pain are common early warning signs of oral and pharyngeal cancer.
- Red patches (erythema) could be seen in the first phases.
- Ulcers, which usually manifest as round or linear yellow/white plaques, form rapidly from the red spots and cause significant discomfort. The insides of the mouth and cheeks, the sides and base of the tongue, and the lips are the most common sites of infection.
- Large, widespread ulcers may cause excruciating agony that makes it impossible to eat or drink, whereas smaller ulcers may just cause moderate discomfort. (To provide the patient's sustenance and hydration under such extreme conditions, feeding tubes may be necessary.) [3]



Cisplatin

One common chemotherapeutic drug is cisplatin, which is also known as cisplatinum or cis-diamminedichloroplatinum (II). Many different types of cancer, including those of the bladder, lungs, head and neck, ovaries, and testicles, have responded to this medicine. Several forms of cancer, including as sarcomas, lymphomas, carcinomas, and germ cell tumors, are effectively combated by it. [4]

Mechanism of Action of Cisplatin

Cisplatin exerts its cytotoxic effects by covalently binding to purine bases, primarily guanine and adenine. This interaction leads to the formation of intra-strand and inter-strand cross-links, resulting in DNA strand breaks. Despite cellular DNA repair mechanisms, persistent damage to DNA, RNA, and proteins can induce apoptosis or other forms of cell death.[5]

Step 1: Cellular Uptake

Cisplatin enters cells mainly via passive diffusion, though active transport mechanisms also contribute:

- Copper transporters (CTR1): Enhance intracellular uptake.
- Organic cation transporters (OCT2): Facilitate entry, particularly in renal cells, contributing to nephrotoxicity.

Step 2: Intracellular Activation (Aquation Reaction)

Inside the cell, cisplatin undergoes hydrolysis due to the low intracellular chloride concentration (~4 mM in the cytoplasm vs. ~100 mM in the bloodstream). This process replaces chloride (Cl^-) ligands with water (H_2O) molecules, generating a highly reactive platinum complex.

Activation reaction:

[PtCl2(NH3)2]+H2O→[Pt(H2O)2(NH3)2]2++2 Cl−\text{[PtCl}_2\text{(NH}_3\text{)}_2\text{]} + H_2O \rightarrow \text{[Pt(H}_2\text{O)}_2\text{(NH}_3\text{)}_2\text{]}^{2+} + 2Cl^-[PtCl2(NH3)2]+H2 O→[Pt(H2O)2(NH3)2]2++2Cl−

The activated platinum complex is electrophilic and readily binds to nucleophilic sites on DNA.

Step 3: DNA Binding and Cross-Linking

The reactive cisplatin derivative binds to the N7 position of guanine bases, leading to DNA cross-link formation:

1. Intrastrand cross-links (~90% of lesions): Bonds form between adjacent guanine (G-G) or guanine-adenine (G-A) bases.
2. Interstrand cross-links (less common but more cytotoxic): Connections occur between guanine bases on opposite DNA strands, resulting in double-strand breaks.
3. DNA-protein cross-links: Cisplatin also binds nuclear proteins, interfering with DNA repair enzymes.

These modifications cause structural distortions in DNA, preventing transcription and replication.

Step 4: Activation of the DNA Damage Response (DDR) Pathway

Cells detect DNA damage and activate DDR pathways to repair lesions or initiate cell death. Key proteins involved include:

- ATM (Ataxia Telangiectasia Mutated) and ATR (Ataxia Telangiectasia and Rad3-related protein): Recognize DNA damage.
- p53 activation: If repair fails, p53 promotes apoptosis.

Step 5: Cell Cycle Arrest and Apoptosis

1. Cell Cycle Arrest: Cisplatin-induced DNA damage halts the cell cycle at the G2/M phase, preventing mitosis.

2. Apoptotic Pathway Activation: If the damage is irreparable, apoptosis is triggered through the mitochondrial pathway:

- p53 activation → Upregulation of pro-apoptotic proteins (BAX, BAK).

- Cytochrome c release → Activation of caspases, leading to programmed cell death.

3. Necrosis (at high doses): Excessive DNA damage may overwhelm the apoptotic pathways, resulting in necrosis.

Step 6: Cellular Detoxification and Cisplatin Resistance

Some cancer cells develop resistance through:

1. Efflux mechanisms: ATP7A/ATP7B copper transporters pump cisplatin out of the cell.
2. Detoxification: Glutathione (GSH) and metallothioneins bind to and neutralize cisplatin.
3. Enhanced DNA repair: Some tumors increase nucleotide excision repair (NER) activity, counteracting cisplatin-induced DNA damage.

Pathophysiology of cisplatin drug induced oral mucositis:

[Cisplatin Administration]

Chemotherapeutic agent administered

↓

[Direct Cellular Damage]

"DNA cross-links → apoptosis of oral mucosal basal epithelial cells"

↓

[ROS Generation]

"Oxidative stress via reactive oxygen species damages cellular components"

↓

[Inflammatory Cascade]

"NF-κB activation → release of TNF-α, IL-1β, IL-6"

↓

[Immune Cell Recruitment]

"Cytokines recruit immune cells, amplifying inflammation"

↓

[Mucosal Barrier Disruption]

"Impaired regeneration → thinning, erythema, ulceration"

↓

[Feedback Loops] ----------> [Back to Inflammatory Cascade]

"DAMPs perpetuate inflammation, delay healing"

↓

[Secondary Complications]

"Infections, myelosuppression impair repair"

↓

[Clinical Manifestations]

"Pain, erythema, ulceration, difficulty eating/swallowing (peaks 7–14 days)"

Pharmacokinetics and Plasma Concentration:

- Cisplatin's plasma concentrations decay mono exponentially, with a half-life of around 20 to 30 minutes after bolus administration (50 or 100 mg/m² doses). This same pattern is observed following 2-hour or 7-hour infusions.
- Total-body clearance and steady-state volume of distribution for cisplatin are around 15 to 16 L/h/m² and 11 to 12 L/m², respectively, after a 100 mg/m² infusion.[6]

Chemical Stability and Metabolism:

- Cisplatin undergoes chemical displacement reactions by nucleophiles (e.g., water, sulfhydryl groups), especially at physiological pH, resulting in the formation of monohydroxy monochloro cis-diammine platinum (II), a major metabolite.
- The cisplatin to free platinum ratio in plasma can vary widely (0.5 to 1.1) after a 100 mg/m² dose.

Protein Binding:

- Cisplatin does not exhibit reversible binding to plasma proteins like most drugs. However, its platinum component binds to albumin, transferrin, and gamma globulin, forming stable complexes.
- After administration, about 90% of plasma platinum is protein-bound within 3 hours, and the platinum-albumin complex has a half-life of 5 days or more.

Tissue Distribution:

- Cisplatin is distributed widely in tissues, with the highest concentrations found in the liver, prostate, and kidney. It accumulates in tissues for as long as 180 days after the last dose.
- Platinum concentrations in tumors are usually lower than in the corresponding tissue (e.g., liver metastases have platinum concentrations similar to normal liver).

Urinary Excretion:

- A significant portion of the administered platinum is excreted in the urine. 10% to 40% of the administered platinum is recovered in the first 24 hours after a dose.
- The parent compound cisplatin is excreted in the urine, accounting for 13% to 17% of the dose in the first hour after administration.
- The renal clearance of cisplatin exceeds creatinine clearance, indicating active renal secretion of platinum-containing molecules.

Renal Clearance and Variability:

- Renal clearance of free platinum varies based on dose, urine flow, and individual variability in secretion and reabsorption.
- Nonlinear renal clearance of free platinum may lead to accumulation when cisplatin is administered daily, but not with intermittent dosing.

Fecal Excretion:

Fecal excretion of platinum appears to be insignificant, with only small amounts of platinum found in the bile and large intestine.

Adult dosing for common indication:

A. **Solid Tumors:**

Single-agent therapy:

o 50–100 mg/m² IV every **3–4 weeks**

o Alternative: 15–20 mg/m² IV **daily for 5 days** every **3–4 weeks**

Combination therapy (most common regimen):

o 20–75 mg/m² IV on Day 1 of a 21- or 28-day cycle
o OR 15–20 mg/m² IV daily for 5 days in a 21-day cycle

B. Testicular Cancer (BEP Regimen)

- 20 mg/m² IV on Days 1–5 of a 21-day cycle
- Usually combined with bleomycin & etoposide
- Total of 4 cycles

C. Ovarian Cancer

- 50–75 mg/m² IV on Day 1 of a 21-day cycle
- Often combined with paclitaxel

D. Bladder Cancer

- 50–70 mg/m² IV every 3–4 weeks
- In combination with methotrexate & vinblastine (MVAC regimen)[17]

Paediatric Dosing:

Solid Tumors:

o 20 mg/m² IV on **Days 1–5** of a **21-day cycle**
o OR **80 mg/m² IV** on **Day 1** of a **28-day cycle**

Management:

1. Preventive Strategies

Palifermin (Keratinocyte Growth Factor-1, KGF-

1): FDA-approved for prevention; stimulates epithelial cell proliferation.

- Cryotherapy (Ice Chips): Reduces cisplatin uptake by oral mucosal cells, minimizing damage.
- Amifostine: A cytoprotective agent that reduces mucosal toxicity.
- Low-Level Laser Therapy (LLLT): Reduces severity by promoting tissue repair and reducing inflammation.

2. Symptomatic Management

A. Pain Management

- Topical Anesthetics:
- Lidocaine (2% viscous solution): Provides temporary relief.
- Benzocaine gel: Numbs mucosal tissue.
- Systemic Analgesics:
- NSAIDs (e.g., ibuprofen) or Acetaminophen: Mild to moderate pain.
- Opioids (e.g., morphine, fentanyl patches): Severe pain

B. Anti-Inflammatory Agents

Corticosteroids (e.g., Dexamethasone mouth rinse): Reduces inflammation and ulceration.

C. Mucosal Healing Agents

Sucralfate Suspension: Forms a protective barrier over ulcers.

Honey: Has anti-inflammatory and wound-healing properties.

Zinc Sulfate Supplementation: May accelerate healing.

D. Antiseptic & Antimicrobial Therapy

Chlorhexidine Mouthwash (0.12% solution): Prevents secondary infections.

Povidone-Iodine Gargle: Reduces microbial colonization.

Systemic Antibiotics: Only if bacterial superinfection occurs.

E. Saliva Substitutes & Coating Agents

Artificial Saliva Sprays: For xerostomia management.

Hydroxypropyl Methylcellulose (HPMC): Coats mucosal surfaces for relief.

3. Adjunctive Therapies

Glutamine Supplements: May reduce mucositis severity.

Probiotics (e.g., Lactobacillus species): Maintain oral microbiome balance.

Adverse Reactions / Toxicity of Cisplatin:

1. Nephrotoxicity (Kidney Damage)

- Major dose-limiting toxicity: Occurs in 28%-36% of patients receiving a single dose (50 mg/m²).
- Manifestations: Elevated BUN, creatinine, uric acid, and reduced creatinine clearance.
- Cumulative toxicity: Becomes worse with repeated doses.
- Risk Factors: Elderly patients and those with pre-existing renal impairment are more susceptible.
- Prevention: Hydration and mannitol diuresis may reduce risk, but toxicity can still occur.

2. Ototoxicity (Hearing Loss)

- Observed in up to 31% of patients after a single dose (50 mg/m²).
- Symptoms: Tinnitus and high-frequency hearing loss (4000-8000 Hz).
- Children at higher risk (40%-60% prevalence).
- Can be unilateral or bilateral and may not be reversible.

Risk Factors:

o Prior cranial irradiation
o Use of other ototoxic drugs (e.g., aminoglycosides, vancomycin)
o Renal impairment
o Age under 5 years

Genetic predisposition: Variants in TPMT gene may contribute to increased susceptibility.

3. Hematologic Toxicity (Blood Disorders)

- Myelosuppression in 25%-30% of patients.
- Leukopenia (low WBCs) & thrombocytopenia (low platelets) peak at days 18-23 and recover by day 39.
- Anemia (drop of 2 g/dL hemoglobin) occurs at a similar rate.
- Serious risks: Severe infections, neutropenia-related fatalities, hemolytic anemia, acute leukemia.
- Higher susceptibility in elderly patients.

4. Gastrointestinal Toxicity

- Severe nausea and vomiting occur in nearly all patients.
- Starts 1-4 hours post-dose, lasting up to 24 hours.
- Delayed vomiting can persist for a week.
- Diarrhea was also reported.

5. Neurotoxicity (Nerve Damage)

- Peripheral neuropathy: Common after 4-7 months of therapy but may occur after a single dose.
- Symptoms include paresthesia, muscle cramps, loss of reflexes.
- May progress even after stopping the drug.

- Possible irreversible damage.

Other neurological effects:

o Lhermitte's sign (electric shock-like sensations)
o Autonomic neuropathy
o Cognitive impairment
o Seizures
o Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

6. Vascular Toxicity

- Can lead to heart attacks, strokes, thrombotic microangiopathy (HUS), cerebral arteritis.
- May be linked to hypomagnesemia.
- Raynaud's phenomenon reported in combination therapy with bleomycin/vinblastine.

7. Electrolyte Disturbances

- Hypomagnesemia, hypokalemia, hypocalcemia, hyponatremia, hypophosphatemia.
- Tetany reported in cases of severe hypocalcemia.
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH).

8. Hyperuricemia (Elevated Uric Acid)

- Common with doses >50 mg/m².
- Peaks at 3-5 days post-treatment.
- Allopurinol can reduce uric acid levels.

9. Ocular Toxicity

- Optic neuritis, papilledema, cerebral blindness.
- Blurred vision & color perception changes (affecting the blue-yellow axis).

10. Anaphylactic Reactions

- Can occur within minutes of administration.
- Symptoms: Facial swelling, wheezing, tachycardia, hypotension.
- Requires immediate emergency intervention (epinephrine, corticosteroids, antihistamines).

11. Hepatotoxicity

- **Elevated liver enzymes (SGOT, bilirubin)**.
- Typically **transient**.

12. Miscellaneous Effects

- Cardiac issues, rash, alopecia, hiccups, dehydration, malaise.
- Extravasation injury (if the drug leaks outside the vein, it can cause severe local tissue damage).

Contraindications:

1. Hypersensitivity to Cisplatin or Other Platinum Compounds – Patients with a history of severe allergic reactions to cisplatin, carboplatin, or oxaliplatin.
2. Severe Renal Impairment – Since cisplatin is nephrotoxic, it is contraindicated in patients with creatinine clearance < 60 mL/min.
3. Severe Myelosuppression – Patients with significantly low white blood cell (WBC), hemoglobin, or platelet counts.
4. Severe Hearing Loss (Ototoxicity) – Patients with pre-existing hearing impairment, as cisplatin is ototoxic and can cause irreversible hearing loss.
5. Pregnancy and Lactation – Teratogenic effects have been observed; contraindicated in pregnant women and nursing mothers.
6. Severe Neuropathy – Cisplatin can worsen peripheral neuropathy, leading to further neurological complications.

Case report:

A male patient with laryngeal cancer, who was 60 years old, was admitted to the oncology department for treatment. The CAP protocol dictated that he receive chemotherapy with cisplatin, doxorubicin, and 5-fluorouracil. Over the course of 90 minutes, the patient was given an intravenous dosage of 60 mg of cisplatin mixed with 500 mL of normal saline. Indicators of oral mucositis appeared during the induction of the fourth cycle of chemotherapy, which occurred after the third cycle had ended. His vitals were as follows: oxygen saturation 97% on room air, temperature 101°F, heart rate 82 bpm, and blood pressure 110/80 mmHg. The results of the tests for the heart and lungs were normal. The patient was diagnosed with Grade 3 oral mucositis according to the World Health Organization's classification after a physical examination revealed a tiny red and swollen area in the tonsillar fossa region. The patient was managed with intravenous granisetron (1 mg/kg) for nausea prevention, dexamethasone (12 mg/kg) to reduce inflammation, and pantoprazole (50 mg IV) for gastroprotection. Supportive care, including hydration and oral hygiene measures, was advised to prevent further mucosal damage. The case study emphasizes the significance of identifying and promptly treating chemotherapy-induced mucositis, as well as the relevance of supportive care, anti-inflammatory medication, and potential adjustments to chemotherapy in enhancing patient outcomes. Close monitoring and proactive intervention are essential to prevent severe complications and maintain the continuity of cancer treatment.

Summary: Oral mucositis (OM) is a common and severe side effect of radiation and chemotherapy that causes painful ulcerative sores on the mouth lining and is marked by redness and inflammation. According to the Common Terminology Criteria for Adverse Events (CTCAE), OM might range from a little reddening of the skin to a potentially fatal necrosis of the tissues. Cisplatin, 5-fluorouracil, and methotrexate are among the most important chemotherapeutic drugs that might cause OM. The platinum-based chemotherapeutic agent cisplatin causes cell death by DNA cross-link formation, which impedes DNA replication and transcription. Negative effects on the kidneys, ears, blood, digestive system, and nervous system are some of the serious side effects that restrict its usage in clinical settings. Grade 3 OM developed in a 60-year-old male patient receiving CAP chemotherapy for laryngeal cancer; in this instance, anti-inflammatory and supportive medicines were used to address the condition. This case underscores the need for effective preventive and therapeutic strategies to mitigate OM severity in patients receiving chemotherapy.

DISCUSSION: OM significantly impacts cancer patients' quality of life, often leading to treatment modifications, nutritional deficiencies, and increased infection risk. The pathophysiology of cisplatin-induced OM involves DNA damage, oxidative stress, and inflammatory responses that impair mucosal integrity. The clinical presentation varies from mild erythema to severe ulceration and hemorrhage, with symptoms such as pain, dysphagia, and secondary infections. Effective management of OM includes both preventive and symptomatic strategies. Preventive measures such as palifermin, cryotherapy, and amifostine aim to reduce mucosal injury. Symptomatic treatment includes pain management with topical anesthetics and systemic analgesics, anti-inflammatory agents like corticosteroids, mucosal healing agents such as sucralfate, and antimicrobial therapy to prevent secondary infections. Adjunctive therapies, including glutamine supplementation and probiotics, may also play a role in reducing mucositis severity. The case report highlights the necessity of early recognition and intervention in OM to prevent complications and maintain

chemotherapy efficacy. Cisplatin's toxicities extend beyond mucositis, necessitating careful monitoring of renal function, auditory capacity, and hematologic parameters. The risk-benefit balance of cisplatin-based regimens must be continuously assessed, with dose modifications considered for patients experiencing severe adverse effects. Supportive care plays a crucial role in mitigating toxicity while ensuring optimal oncologic outcomes.

CONCLUSION:

Oral mucositis remains a major complication of chemotherapy, particularly with agents like cisplatin. Its management requires a multidisciplinary approach incorporating preventive, symptomatic, and supportive strategies. Early identification and prompt intervention can improve patient outcomes, minimize treatment disruptions, and enhance overall quality of life. Future research should focus on novel therapeutic agents and targeted approaches to reduce mucositis incidence and severity while preserving the antineoplastic efficacy of chemotherapy regimens.

REFERENCES

1. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Bethesda, MD: U.S. Department of Health and Human Services; 2017.
2. Sonis ST. Oral mucositis in cancer therapy. J Support Oncol. 2004;2(6 Suppl 3):3–8.
3. Peterson DE, Boers-Doets CB, Bensadoun RJ, Herrstedt J. Management of oral and gastrointestinal mucositis: ESMO Clinical Practice Guidelines. Ann Oncol. 2015;26(Suppl 5):v139–v151.
4. Wang D, Lippard SJ. Cellular processing of platinum anticancer drugs. Nat Rev Drug Discov. 2005 Apr;4(4):307–20.
5. Galluzzi L, Senovilla L, Vitale I, Michels J, Martins I, Kepp O, et al. Molecular mechanisms of cisplatin resistance. Oncogene. 2012 Nov;31(15):1869–83.
6. Dasari S, Tchounwou PB. Cisplatin in cancer therapy: Molecular mechanisms of action. Eur J Pharmacol. 2014 Oct;740:364–78.
7. Florea AM, Büsselberg D. Cisplatin as an anti-tumor drug: Cellular mechanisms of activity, drug resistance and induced side effects. Cancers (Basel). 2011 Dec;3(1):1351–71.
8. Miller RP, Tadagavadi RK, Ramesh G, Reeves WB. Mechanisms of Cisplatin nephrotoxicity. Toxins (Basel). 2010 Nov;2(11):2490–518.
9. Siddik ZH. Cisplatin: Mode of cytotoxic action and molecular basis of resistance. Oncogene. 2003 Oct;22(47):7265–79.
10. Sonis ST. Pathobiology of oral mucositis: novel insights and opportunities. J Support Oncol. 2007 Mar;5(9 Suppl 4):3–11.
11. Lalla RV, Bowen J, Barasch A, Elting L, Epstein J, Keefe DM, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2014 May;120(10):1453–61.
12. Peterson DE, Bensadoun RJ, Roila F. Management of oral and gastrointestinal mucositis: ESMO Clinical Practice Guidelines. Ann Oncol. 2011 Sep;22(Suppl 6):vi78–84.
13. Wang D, Lippard SJ. Cellular processing of platinum anticancer drugs. Nat Rev Drug Discov. 2005 Apr;4(4):307–20.
14. Dasari S, Tchounwou PB. Cisplatin in cancer therapy: molecular mechanisms of action. Eur J Pharmacol. 2014 Oct;740:364–78.
15. Miller RP, Tadagavadi RK, Ramesh G, Reeves WB. Mechanisms of Cisplatin nephrotoxicity. Toxins (Basel). 2010 Nov;2(11):2490–518.

16. Florea AM, Büsselberg D. Cisplatin as an anti-tumor drug: cellular mechanisms of activity, drug resistance and induced side effects. Cancers (Basel). 2011 Dec;3(1):1351–71.
17. Siddik ZH. Cisplatin: mode of cytotoxic action and molecular basis of resistance. Oncogene. 2003 Oct;22(47):7265–79.
18. Boulikas T, Vougiouka M. Cisplatin and platinum drugs at the molecular level. Oncol Rep. 2003 Oct;10(6):1663–82.
19. Pabla N, Dong Z. Cisplatin nephrotoxicity: mechanisms and renoprotective strategies. Kidney Int. 2008 Dec;73(9):994–1007.
20. Ruggiero A, Trombatore G, Triarico S, Arena R, Scalzone M, Battista A, et al. Platinum compounds in children with cancer: toxicity and clinical management. Anticancer Drugs. 2013 Oct;24(9):1007–19.
21. Langer CJ, Manola J, Bernardo P, Kugler JW, Bonomi P, Cella D, et al. Cisplatin-based therapy for elderly patients with advanced non–small-cell lung cancer: implications of Eastern Cooperative Oncology Group 5592, a randomized trial. J Natl Cancer Inst. 2002 Apr;94(3):173–81.
22. Rybak LP, Mukherjea D, Ramkumar V. Mechanisms of cisplatin-induced ototoxicity and prevention. Semin Hear. 2019 May;40(2):197–204.
23. McKeage MJ. Comparative adverse effect profiles of platinum drugs. Drug Saf. 1995 Sep;13(4):228–44.
24. Bokemeyer C, Berger CC, Hartmann JT, Kollmannsberger C, Schmoll HJ, Kuczyk MA, et al. Analysis of risk factors for cisplatin-induced ototoxicity in patients with testicular cancer. Br J Cancer. 1998 May;77(8):1355–62.
25. Feldman DR, Bosl GJ, Sheinfeld J, Motzer RJ. Medical treatment of advanced testicular cancer. JAMA. 2008 Mar;299(6):672–84.
26. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Bladder Cancer. Version 2.2024.
27. Arany PR, Nayak RS, Hallikeremath SC, Bhadra shetty D, Patil CS, Suresh DK. Low-level laser therapy for treatment of oral mucositis induced by chemotherapy: a systematic review. Lasers Med Sci. 2015 Jul;30(5):1305–13.
28. Clarkson JE, Worthington HV, Furness S, Eden TOB. Interventions for treating oral mucositis for patients with cancer receiving treatment. Cochrane Database Syst Rev. 2010 Aug;(8):CD001973.
29. Lexicomp Online, Lexi-Drugs [database on the Internet]. Hudson (OH): Wolters Kluwer Health; 2024 [cited 2025 Apr 22]. Available from: http://online.lexi.com
30. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Antiemesis, Kidney Cancer, and Testicular Cancer [Internet]. Plymouth Meeting (PA): NCCN; 2024 [cited 2025 Apr 22]. Available from: https://www.nccn.org
31. British National Formulary (BNF). Cisplatin – contraindications and cautions [Internet]. London: BMJ Group and Pharmaceutical Press; 2024 [cited 2025 Apr 22]. Available from: https://bnf.nice.org.uk.

HOW TO CITE: Reyaz Golsangi*, Samreen, Asha Raj, Vedant Bhoskar, Mohd Shahnawaz, Shaik Umair, Sayed Omer Ahmed, Ramaiah Medical College Teaching Hospital, Int. J. of Pharm. Sci., 2025, Vol 3, Issue 4, 3449-3459 https://doi.org/10.5281/zenodo.15310395