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Review Article

Recent And Advance Study On Anticancer Drugs

Rutuja P. Nirmal*[1], Rutuja Jogdande[2], Jaya Kamble[3], Pritam Solakhe[4] ,Nilesh B. Chougule[5]

[1-2]*Student Ashorao Mane Institue of Pharmacy, Ambap-416112*
[3-4]*Assistant Professor Ashokrao Mane Institue of Pharmacy, Ambap.*
[5]*Principal Ashorao Mane Institue of Pharmacy, Ambap*

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ABSTRACT

In this review, we address some of the current issues and the potential for the future of cancer therapy while highlighting the key concepts. Globally, cancer is the main issue pertaining to public health.Radiation, surgery, and chemotherapy are the most prevalent kinds of cancer treatments that are currently offered. Both Carboplatin and Paclitaxel are commonly used anti-cancer medications, but they work in different ways.Many cancers, such as those of the breast, ovaries, lungs, brain, and prostate, are treated with paclitaxel. Carboplatin is a platinum-based chemotherapy drug that is frequently used to treat a variety of cancers, such as cervical, endometrial, ovarian, lung, thyroid, head and neck, uterine, germ cell tumor, and upper gastrointestinal tract cancer.

INTRODUCTION

Globally, cancer is a significant public health issue. Demographic factors indicate that the incidence of cancer will decline over the next few decades, with an estimated 420 million new cases annually by 2025. GLOBOCAN data shows that 14.1 million new cases and 8.2 An estimated million people died from cancer in 2012[1].In Europe, the most common cancers diagnosed are those of the female breast, colorectal, prostate ,and lung[2]. Today, the most widely used cancer treatments are chemotherapy, surgery, and radiation. Although chemotherapy has been around since the early 1900s, its application in the treatment of cancer did not start until the 1930s. The phrase "chemotherapy" was initially used by the Paul Ehrlich, a German scientist witha special interest in alkylating agents, coined the phrase to refer to the chemical treatment of illness. It Alkylating medications, like chlorambucil and cyclophosphamide, were created in the ensuing yearstocombat cancer was discovered that soldiers exposed to mustard gas during World Wars I and II had lower leukocyte counts. This resulted in the 1943 treatment of lymphomas by Gilman with nitrogen mustard, which was the first

***Corresponding Author:** Rutuja P. Nirmal
Address: *Student Ashorao Mane Institue of Pharmacy, Ambap-416112.*
Email : rutujanirmal17@gmail.com
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chemotherapy agent[3,4]. Methotrexate was developed in 1948 after Kilte and Farber created folate antagonists like aminopterin and amethopterin, which helped children with leukaemia achieve remission [5]. In 1951, Elion and Hitchings created 6-mercaptopurine and 6-thioquanine for Leukaemia treatment [6,7].Every year, more than ten million people receive a cancer diagnosis [8].A large range of disorders are collectively referred to as cancers, and they are all distinguished by multiplet abnormal and continuous cell growth in a particular tissue site, which gives rise to the tumor [9]

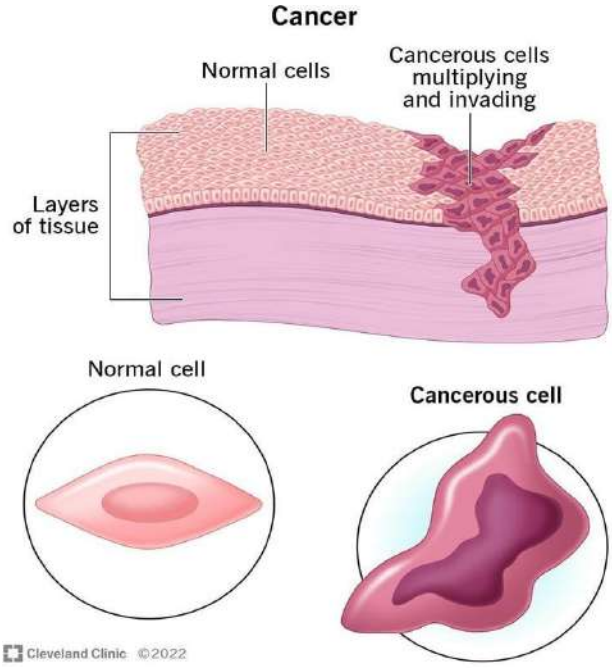

Fig.no. 1 Cancer Cell

I. Paclitaxel:-

Hydrobhobic Paclitaxel is an anticancer drug that works well for treating lung,ovarian, breast, and as well as cancer of the head and neck. Paclitaxel is formulated with the micelle-forming vehicle Cremophor EL to improve drug solubility due to its insolubility in water[11].

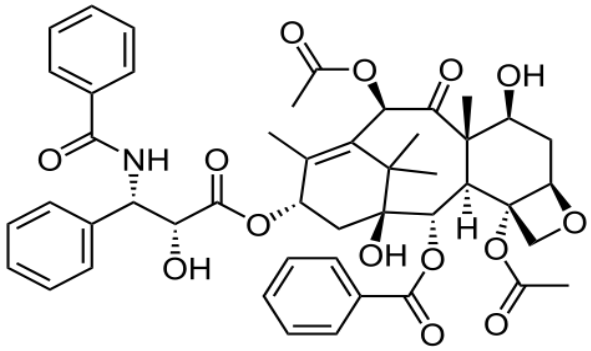

Fig.no. 2 Structure of Paclitaxel

A. Category Of Paclitaxel :-

Chemotherapeutic Agent , Antimicrotubular agent.

B. Mechanism of action:-

The use of paclitaxel as an anticancer medication has been reported to have the capacity to target microtubules. In 3 nature, microtubules have a cylindrical hollow body shape with a diameter ranging from 25 to 30 nm. which is composed of tubulin heterodimers, which contain beta and alpha components of the protein subunits, and multiple tubulin polymers that are in dynamicequilibrium[13.,14].

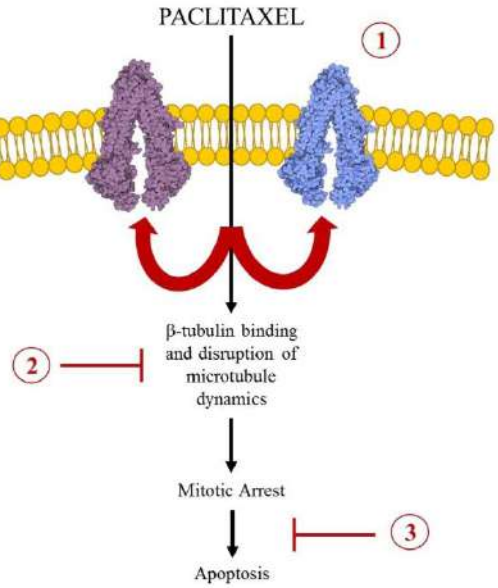

Figure 3. The Major Mechanisms of Paclitaxel Resistance. The cellular mechanism of action by which paclitaxel serves as an anticancer drug, as illustrated following the black arrows. Paclitaxel enters the cell and binds to b-tubulin on the inner

surface of microtubules. This stabilizes the microtubule network, arrests the cell cycle at the G2/M phase, and therefore leads to apoptosis. Cancer cells have been found to evade the microtubule stabilizing action of paclitaxel through three main mechanisms (illustrated in red): (1) over-expression of transmembrane efflux transporters, specifically ABCB1 and ABCC10; (2) tubulin mutations (both α and β) or alterations in the stability of the microtubule network; and (3) reduced function of significant apoptotic proteins, such as Bcl-2 and p53.] [15].

D**. Paclitaxel in cancer therapy:-**

1. Breast cancer:-

Paclitaxel has emerged as an important agent in treatment of breast cancer. Paclitaxel is active in treatment of metastatic breast canceras first line tharapy.[16,18] as well as in heavily pretreated patients[17,19,21].Especially Encouraging is its activity in anthracycline resistant disease[21,22].

2. Ovarian cancer:-

Ovarian cancer is the fifth most common cause of cancer-related deaths in women worldwide, and its prevalence is rising quickly. An estimate states that one in every 70 The majority of females who develop ovarian cancer pass away from it [20]. Paclitaxel has been recommended forth treatment of ovarian cancer in recent years [23]. After 28 patients with ovarian cancer received weekly intraperitoneal chemotherapy at a dose of 60mg/m2,the disease's median recurrence time was found to be 25 months, with mild toxicity in11% of the patients[31].Bae and colleagues evaluated the feasibility and efficacy of giving Paclitaxel or carboplatin to patients with advanced ovarian cancer during intraperitoneal hyperthermic chemotherapy(IPHC)[32].

3. Lung cancer:-

Lung cancer is one of the main causes of death in the world. While the number of lung cancer-related deaths in the US and the UK has declined and the number of survivors has increased, the incidence and mortalityof lung cancer in Since the number of developing nations is rising, considerable effortsare needed to lower the death rate from lung cancer [24]. Extended weekly administration of paclitaxel has been achieved in disseminated non-small cell lung cancer(NSCLC) trials (phase I and II) to evaluate its effect on DI (dose intensity) limits and tolerability in experimental subjects. Weekly doses of paclitaxel ranging from 100 to 200 mg/m2 were used in the Phase-I trial. Phase-II trials administered paclitaxel at the maximum tolerated dose of 175 mg/m2. Paclitaxel (3-hour infusion/week) was found to be active in the patients examined in this study and demonstrated impact on their platelets that is protective [25].

4. Brain cancer:-

The leading cause of death for children under the age of 19 is brain cancer. Glioblastoma is the most dangerous kind of brain tumor and Is also very resistant to anti-tumor medications [26].Due to paclitaxel's inadequate penetration throught the blood-brain barrier, this medication's efficacy is minimal. The blood-brain barrier was quickly broken down by low-intensity pulsed ultrasound (LIPU) and microbubble injection,which improved paclitaxel delivery to the brain.Inpre-clinical gliomamodels,the impact of administering paclitaxel with LIPU assistance(nab-paclitaxel and cremophor-paclitaxel)has been assessed.In conclusion,it was discovered that paclitaxel delivered with LIPU assistance was more successful in treating gliomas.When comparing the two formulations under investigation, nab-paclitaxel had a more significant impact than cremophor-paclitaxel [27].

5. Prostate cancer:-

Prostate cancer is the second most common cause of death for men worldwide among all cancers [28]. According to a study with thirty-two patients who received intravenous 100 mg of paclitaxel in addition to other medications,

(intravenous100mg/m2)estramustin phosphate (oral 10 mg/kg) and carboplatin produced a successful treatment for prostate cancer that was hormone-refractory [29]. The proliferation of DU145prostate cancer cells was effectively inhibited by paclitaxel-loaded nano-fiber mats,as evidenced by the results of cell culture. Prostate cancer treatment was suitable for chitosan-hyaluronic acid fibers because they influenced the controlled release of paclitaxel [30].

E. Paclitaxel formulation in clinic:-

The Food and Drug Administration(FDA) in the United States has only recently approved two PTX-based chemotherapy treatments: Abraxane® and Taxol®.These are called PTX Formulations in Clinic. Although both formulations are meant to be administered intravenously, they have different combining agents. Unlike Abraxane®,which uses albumin to stabilize PTX,Taxol®uses a combination of Cremophor ELand dehydrated ethanol (49.7%,v/v)[33]. Liposomal PTX(Lipusu®)has received approval for clinical use in China[34, 35].

1. Taxol:-

Bristol-Myers-Squibb introduced Taxol®,the first authorized form of PTX,on to the market in1992.Six milli liters of PTX are dissolved in each milli liter of the Taxol® formulation,which is composed of49.7% ethanol and 527 mg of polyoxyethylated castor oil,or Cremophor EL.[36] usually,Taxol® administered by 3 or 24-hour infusion following dilution with a fluid that is balanced.Table 1displays the typical pharmacokinetic parameters of Taxol®dosed at 175 mg/m2 following a 3-hour intravenous fusion.It is currently approved to treat ovarian cancer, non-small cell lung cancer,primary and metastatic breast cancer, and Kaposi's sarcoma associated with AIDS.[37] Along with PTX-induced nephrotoxicity and neurotoxicity, Taxol®'s non-linear pharmacokinetics and hypersensitivity represent significant drawbacks in its clinical use.[36] For example, when 135 or 175 mg/m2 of Taxol® was given by 30% dosage increase after three hours of infusion can actually result in an 89% increase in

Fig. no. 3 Taxol

AUC0-∞ and a 68% increase in Cmax. Patients receiving Taxol® treatment should be premedicated with corticosteroids, diphenhydramine, and H2 antagonists to reduce severe hypersensitivity reactions. It is thought that the use of CremophorEL is the cause of these problems: 1) AUC0-∞ increases non-proportionally when cremophor EL forms micelles in blood at high concentrations and traps PTX in the hydrophobic Core [38]. and 2) The complement system may be triggered by cromatophorEL.high dosages of histamine activation and release.[39, 40] Longer infusion times are frequently required to reduce the negative effects of Cremophor EL-rooted medication. These restrictions had inspired Manufacturers and researchers should look for PTX formulations without Cremophor EL. [fig no .4 Taxol] [46]

2. Abraxane:-

The second PTX formulation utilized in clinical settings is called Abraxane®, and it was created by Abrax is BioScience (later acquired by Celgene). The FDA first approved Abraxane® in 2005 to treat metastatic breast cancer, and later approved it

to treat locally advanced or metastatic pancreatic adenocarcinoma and metastatic non-small cell lung cancer.[41] Human serum albumin is used in the formulation of PTX in Abraxane®. (HAS).[42] HAS, which has a half-life of approximately 19 days, is the most prevalent plasma protein in human blood. It has the ability to bind hydrophobic chemicals reversibly, carry them throughout the body ,and release them at the surface of cells.[43] More over, HAS binds to gp60 to facilitate cellular up take and transcytosis.It also binds to SPARC,a secreted protein that is acidic and rich in cysteine and is known to be highly expressed in cancerous cells and stromal cells linked to in conjunction with neoplasia. The exact amount that HAS's biological functions add to Abraxane®'s higher response rates is still unknown, though. Unquestionably, removing Cremphor EL makes it possible to administer a higher dose of PTX with equivalent toxicities. When compared to Taxol®, Abraxane® has a maximum tolerated dose of 300 mg/m2, and its administration time can be significantly reduced (30 min for Abraxane® versus 3or24 hrforTaxol®).[45] Furthermore, the findings from Abrax is BioSciences indicated that, in comparison to an equal dose injection of Taxol®, Abraxane® increases intratumor PTX concentration by 33% and has a predictable, linear pharmacokinetic profile.Eliminating Cremophor EL also removes the need for special IV tubing and premedication in order to administer Taxol®, as well as hypersensitivity reactions

Fig.no. 4 Abraxane

3. Other approved formulations :-

The first injectable PTX liposome to hitthe Chinese clinical market was Lipusu® ,created by Luye Pharmaceutical Co.Ltd.in 2003. The PTX, lecithin, and cholesterol formulations have been approved for the treatment of ovarian cancer, breast cancer,and lung cancer with non-cells.Lipusu® demonstrated comparable efficaciousness against gastric cancer,non-small cell lung cancers,and breast cancer in comparison to Taxol®,but with noticeably fewer side effects[48,49]. Therefore,Lipusu® may be a good substitute for Abraxane®.The2007 formulation of PTX known as Genexol-PM® was made with poly(ethylene glycol)-b-poly(lacticacid)(PEG-b-PLA)block copolymers and sold by Samyang Corporation. In South Korea, it has been authorized for the therapy for non-small cell,ovarian,and breast cancer.Clinical trials showed that Genexol-PM is well tolerated by patients and has dose-dependent pharmacokinetics, especially for those with advanced pancreatic cancer or metastatic breast cancer[50].

Table 1: Comparison of Taxol® and Abraxane®

	Taxol	**Abraxane**
Formulation	Cremophor EL and dehydrated ethanol	Albumin NPs
Partical size	N/A	~130nm
MTD	240 mg/m²	300 mg / m²
Clinical Dosage	175 mg/m²	260 mg/m²
Administration	i.v 3h	i.v 30 min
VD(L/m²)	227	632
Clearance (L/h/m²)	12 .2	15
Cmax(ng/ml)	3,650	18,741
AUC (h*ng/ml)	15,007	17,434
T½(h)	20.2	27

All values acquired from FDA website. MTD: the maximum tolerated dose; Vd: apparent volume of distribution; Cmax: Maximum Concentration; AUC: plasma area under the curve; t1/2half-

lifetime.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021660s037lbl.pdf

II. Carboplatin:-

A platinum anticancer medication called carboplatin, also known as cis-diammine(cyclobutane-1,1 dicarboxylato)platinum(II), Fig. 1, is used to treat a variety of human cancer types [54–58]. Although the exact chemical mechanism of action of carboplatin is unknown, it is believed to work by interacting with cellular targets such tubulin, genomic DNA, and other proteins to produce its biological effects [59–61].Barnett Rosenberg and others created carboplatin in the early 1970s in an effort to enhance the therapeutic efficacy of cisplatin, also known as cis-diamminedichloroplatinum(II), a first-generation platinum anticancer medication (Fig. 1) [59,62]. Carbaplatin was eventually licensed as a medication in 1989 under the trade name paraplatin as it was discovered to be significantly less oto-, neuro-, and nephrotoxic than cisplatin [54,59,63].

A. **Structure of carboplatin:-**

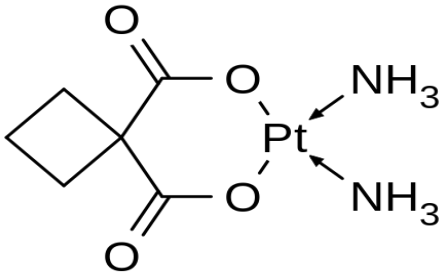

Fig.no. 6 Structure of Carboplatin

B. **Category Of Drug:-**

Antineoplastics, Alkylating , Platinum Analogs

C. **Mechanism of action :-**

As a cisplatin derivative, carboplatin functions similarly but has a different structure and toxicity. Since the FDA gave it approval in the 1980s, it has been extensively utilized to treat a variety of tumor forms. This agent's unique property is its capacity to cause lesions in DNA by forming adducts with platinum, which block transcription and replication and ultimately cause cell death. A[66]

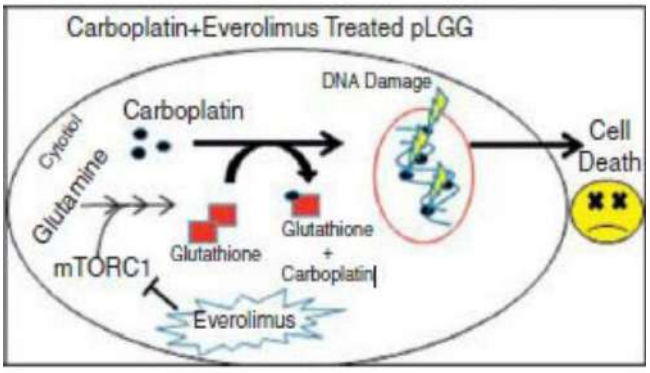

Fig no. 7 Mechanism of action of carboplatin

D. Carboplatin in cancer therapy:-

1. Ovarian cancer;-

Before the mid-1990s, Cyclophosphamide with carboplatin was the usual treatment for advanced-stage ovarian cancer, however some doctors still preferred single-agent carboplatin. Comparative investigations of combinations comprising carboplatin vs cisplatin provided the foundation. There were no differences observed in response rates or survival in the two North American studies comparing carboplatin-cyclophosphamide and cisplatin-cyclophosphamide [67,68].

2. Testicular cancer:-

Testicular cancer was known to be moderately susceptible to chemotherapy before cisplatin was discovered. Dactinomycin was the most effective treatment, producing responses in about 50% of patients, 10% of whom were complete [69]. Merely 5% of the patients experienced recovery. Patients were thus free to participate in studies of novel drugs, and in the first Phase-I trials of cisplatin, patients with testicular malignancies showed responses [70].

3. Lung cancer:-

A randomized ECOG trial indicated that carboplatin therapy was associated with a survival advantage over combination regimens, although it yielded an objective response rate of just 9%. These rather unexpected results were

the outcome of early trials of carboplatin as a single-agent in NSCLC[71]. Compared to cisplatin, carboplatin did show notable single agent activity in SCLC, with response rates that were close to 60% [72].

4. Cancer of the head and neck:-

Researchers from France presented their randomized outcomes utilizing carboplatin-based chemo radio therapy at the 1998 ASCO meeting: 226 patients received radiation alone versus carboplatin (70 mg/m2 daily × 4) and 96-hour infusion of 5-FU every 21 days with radiation. Significantly longer three-year survival was seen in the chemo radio therapy group (51% vs. 31%, p = 0.002) [73]. An absolute survival benefit of 8% for chemo radio therapy in locally advanced head and neck cancer was verified by Bourhis, Pignon et al. in a meta-analysis of 63 randomized trials including over 10,000 patients [74].

5. Urothelial Cancer:-

Cisplatin is a key component of all the most effective combination regimens found to date and is used in the treatment of advanced transitional carcinomas of the bladder. The M-VAC regimen (methotrexate, vinblastine, doxorubicin, and cisplatin), created at Memorial in the 1980s, is the current standard of therapy [75]. Recently published phase II trials have demonstrated the efficacy of carboplatin with paclitaxel. Vaughn & associates [76].

6. Germ cell tumor:-

In a major multicenter trial, etoposide was compared in a randomized fashion with either carboplatin or cisplatin for germ cell malignancies [77]. The scientists came to the conclusion that carboplatin, the conventional first-line platinum analogue for metastatic germ cell cancers, was not as effective as cisplatin in this combination chemotherapy treatment.

7. Upper Gastrointestinal tract cancer :

Cisplatin is a cornerstone of the treatment for esophageal adeno carcinomas and squamous-cell carcinomas.Patients with advanced disease have reported response rates of up to 40% with cisplatin alone. The EORTC observed that when cisplatin was given with 5-FU by continuous infusion as opposed to cisplatin alone, the response rate doubled to 35% from 19% [78–80].

8. Cervical and endometrial Cancer:-

A 15% response rate with carboplatin was observed in the GOG's 1989 report on the outcomes of a sizable randomized trial comparing carboplatin and iproplatin monotherapy. This finding suggested that carboplatin's activity might not be equivalent to that of cisplatin in the treatment of cervical cancer [81].

E. Carboplatin Formulation in clinic :-

1. **CARBOTIN:**

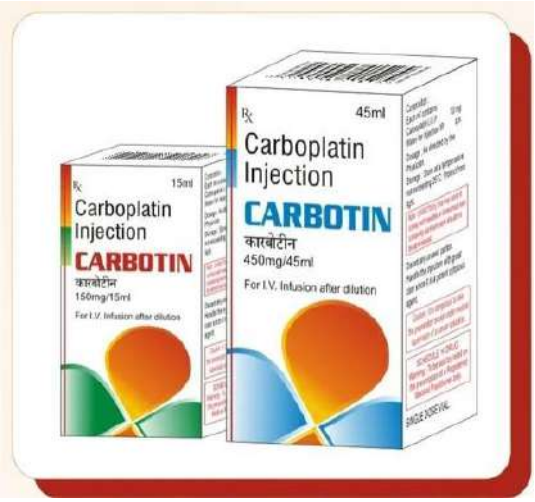

Fig no .8 carboplatin

Used to treat advanced bladder, head, and neck cancer, and also metastatic testicular and reproductive carcinomas .

2. Injection of Carboplatin BP:-

A chemotherapy drug called carboplatin is used to treat many cancer types. This encompasses cancers of the ovaries, lungs, head & neck, brain, and neuroblastoma**.**

Fig no. 9 carboplatin

Stability Testing of Pharmaceutical Products :-

Pharmaceutical stability testing is an intricate process that requires a great deal of money, time, and scientific knowledge in order to ensure that a medicine formulation is safe, effective, and of high quality.

Stability testing methods:-

Stability testing is a common practice used at different phases of product development on medicinal substances and products. Accelerated stability testing, conducted at relatively high temperatures and/or humidity levels, is utilized in the first phases to identify the kinds of degradation products that might be discovered after extended storage.

1. **Real-time stability testing:**

To allow for significant product degradation under advised storage settings, real-time stability testing is typically carried out over a longer test period.

2. **Accelerated stability testing:**

In this type of testing, a product is subjected to many high temperatures (warmer than room temperature) in order to identify the minimum amount of heat input necessary to cause the product to fail. This is done in order to put the product in an environment that speeds up degradation .

3. **Testing for stability of retained samples:**

Every marketed product for which stability data are needed follows this standard procedure. Stability samples that will be kept in storage for at least one batch every year are chosen for this investigation. Stability samples from two batches should be obtained if the number of batches marketed exceeds fifty.

4. **Cycle temperature stress testing:**

This is not a standard testing procedure for goods that are sold. This method involves designing cyclic temperature stress tests based on product knowledge to replicate expected market storage conditions. Since the earth's diurnal rhythm is 24 hours, which marketed medications are most likely to experience during storage, the cycle period is typically considered to be 24 hours.

CONCLUSION

The analysis concludes by highlighting the critical role that Paclitaxel and Carboplatin play as potent anti-cancer medications, especially when treating lung, breast, and ovarian malignancies. The review report concludes by highlighting the encouraging potential of paclitaxel and carbonation as strong anticancer medications. When combined, their distinct methods of action show synergistic benefits, providing a novel approach to cancer treatment. To validate these results and maximize the therapeutic outcomes, more investigation and clinical testing are essential. The combination of paclitaxel with carbonation may lead to better overall patient outcomes, decreased side effects, and increased efficacy in the fight against cancer.[84]

Improving the stability of anticancer drugs:-

The problem of maximizing patient care under the limitations of the pharmacy's resources is one that oncology pharmacists frequently encounter in their line of work. One factor that may cause delays and longer patient wait times is the day's centralized infusion preparation. All parties involved may benefit, though, if this is done beforehand or through outsourcing. Sadly, there are frequently few stability studiesThe authors of the recently released recommendations on the practical stability studies of anticancer

medications noted the need for more stability data encompassing applications of anticancer medications. The manufacturer's given data frequently misrepresents the actual stability of the medications.[85]. Despite the fact that anticancer medications are typically made in centralized units under rigorous aseptic conditions, the manufacturer typically quotes the stability of these drugs as being stable for 8 to 12 hours for bacterial contamination after the dilution phase. As a result, carrying out stability studies on cytotoxic medications will make use of additional information regarding their stability profile and enable weekend or household preparation.Chemotherapy treatment cycles can be planned ahead of time, which can save cancer centers money. Increasing the stability profile of chemotherapy drugs can assist pharmacists in providing patients with a less disruptive regimen and streamlining services, both of which can contribute to a higher quality of life. We read with interest the recently published article‘Long-term stability of clofarabine injection concentrate and diluted clofarabine infusion solution’[86]. It is always interesting to read a stability study of an anticancer drug and observe the storage conditions for the test solutions that will mimic normal clinical practices. It is important to note that these clinical practices will vary from one country to another as some countries’ room temperature could exceed 30C depending on the climate of the country and the air-conditioning facilities available at each hospital.Additionally, anticancer medications could be given to patients through elastomeric portable pumps, making at-home chemotherapy easier. Since the patients will be wearing these pumps and covering them with their clothing, they will be exposed to temperatures greater than the surrounding air, up to or exceeding 37C[87]. The anticancer medication may deteriorate at this higher, unidentified temperature, and unfavorable substances may leak into the solution from the containers or delivering equipmemt. It is necessary to take into account the temperature at which these chemotherapy drugs are exposed. Since cytotoxic medications are known to have a limited therapeutic range, stability tests must be conducted for each anticancer medication while it is being stored under in-use settings. This is because giving patients the appropriate dose is crucial to their prognosis[88]. We are excited to present the results of our most recent and ongoing study on the application of elastomeric pumps to home chemotherapy. By doing so, we will be able to replicate common clinical procedures, such as at-home chemotherapy, and ascertain the anticancer drug's durability at these various temperatures. Furthermore, each anticancer medication will be evaluated separately based on how long it is in contact with the delivering devices and/or containers. The real room temperature of the hospitals or cancer research facility must be taken into consideration when conducting stability studies of cytotoxic medications.

CONCLUSION

In conclusion, the review underscores the pivotal role of Paclitaxel and Carboplatin as formidable anti-cancer drugs, particularly in the treatment of ovarian, lung, and breast cancers . In conclusion, the review paper highlights the promising potential of carbonation and paclitaxel as effective anticancer drugs. Their unique mechanisms of action, when combined, demonstrate synergistic effects, offering a novel approach in cancer treatment. Further research and clinical trials are crucial to validate these findings and optimize the therapeutic outcomes. The integration of carbonation and paclitaxel could pave the way for enhanced efficacy, reduced side effects, and improved overall patient outcomes in the battle against cancer.

REFERENCES

1. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods FERENCES and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359–E386.
2. Ferlay J, Steliarova-Foucher E, Lortet-Tieulent J, et al. Cancer incidence and mortality patterns in Europe: estimates for 40 countries in 2012. Eur J Cancer. 2013;49:1374–1403.
3. Gilman, A. Symposium on advances in pharmacology resulting from war research: Therapeutic applications of chemical warfare agents. Fed. Proc. 1946, 5, 285-292.
4. Goodman, L.S.; Wintrobe, M.M.; Dameshek, W.; Goodman, M.J.; Gilman, A.; McLennan, M.T. Nitrogen mustard therapy: Use of methyl-bis (h-chloroethyl) amine hydrochloride and tris (h- chloroethyl) amine hydrochloride for Hodgkin's disease, lymphosarcoma, leukemia, and certain allied and miscellaneous disorders. JAMA 1946, 132, 126-132.
5. Farber, S.; Diamond, L.K.; Mercer, R.D.; Sylvester, R.F., Jr.; Wolff, J.A. Temporary remissions in acute leukemia in children produced by folic acid antagonist, 4-aminopteroyl-glutamic acid (aminopterin). N. Engl. J. Med. 1948, 238, 787-793.
6. Hitchings, G.H.; Elion, G.B. The chemistry and biochemistry of purine analogs. Ann. N. Y. Acad. Sci. 1954, 60, 195-199.
7. Elion, G.B.; Singer, S.; Hitchings, G.H. Antagonists of nucleic acid derivatives. VIII. Synergism in combinations of biochemically related antimetabolites. J. Biol. Chem. 1954, 208, 477-488.
8. Siegel, R.L.; Miller, K.D.; Fuchs, H.E.; Jemal, A. Cancer Statistics, 2021. CA Cancer J. Clin. 2021, 71, 7–33. [Google Scholar] [CrossRef]
9. Cooper, G.M. The Cell: A Molecular Approach. In The Development and Causes of Cancer, 2nd ed.; Sinauer Associates: Sunderland, MA, USA, 2000. Available online: https://www.ncbi.nlm.nih.gov/books/NBK9963/ (accessed on 1 January 2020).
10. https://my.clevelandclinic.org/health/diseases/12194-cancer
11. Paclitaxel chemotherapy: from empiricism to amechanism-based formulation strategyCharity D Scripture, William D Figg & Alex SparreboomTo cite this article: Charity D Scripture, William D Figg & Alex Sparreboom (2005) Paclitaxelchemotherapy: from empiricism to a mechanism-based formulation strategy, Therapeuticsand Clinical Risk Management, 1:2, 107-114, DOI:10.2147/tcrm.s1210762910To link to this article: https://doi.org/10.2147/tcrm.s121076291
12. https://en.m.wikipedia.org/wiki/Paclitaxel
13. E. K. Rowinsky and R. C. Donehower, "Paclitaxel (Taxol)," The New England Journal of Medicine, vol. 332, no. 15, pp. 1004–1014, 1995.View at: Publisher Site | Google Scholar
14. J. Parness and S. B. Horwitz, "Taxol binds to polymerized tubulin in vitro," The Journal of Cell Biology, vol. 91, no. 2, pp. 479–487, 1981. View at: Publisher Site | Google Scholar
15. https://images.app.goo.gl/KuDZNrESVMs7K8JaA
16. Mamounas E, Brown A, Fisher B et al. 3-hour(hr) high dosetaxol (T) infusion in advanced breast cancer (ABC): an NSAPB phase II study. Proc Am Soc Clin Oncol 1995;14:127.
17. Seidman AD, Tiersten A, Hudis C et al. Phase II trial of paclitaxel by 3-hour infusion as initial and salvage chemotherapyfor metastatic

breast cancer. J Clin Oncol 1995;13:2575-2581.

18. Davidson NG. Single-agent paclitaxel as first-line treatment of metastatic breast cancer: the British experience. SeminOncol 1996;23(suppl 11):6-10.
19. Holmes FA, Valero V, Walters RS et al. The M.D. Anderson Cancer Center experience with taxol in metastatic breast cancer . J Natl Cancer Inst Monogr 1993;15:161_169.
20. Ovarian Cancer in Australia: An Overview, 2010. Australian InstiTute of Health and Welfare and National Breast and Ovarian CanCer Centre (Australia). Cancer SeriesCanberra,Australia: Australi- An Institute of Health and Welfare 2010, p 115-120.
21. Seidman AD, Reichman BS, Crown JP et al. Paclitaxel as second and subsequent therapy for metastatic breast cancer:activity independent of prior anthracycline response. J Clin3 Seidman AD, Tiersten A, Hudis C et al. Phase II trial of pacliOncol 1995;13:1152-1159.
22. Fountzilas G, Athanassiades A, Giannakakia T et al. A phaseII study of paclitaxel in advanced breast cancer to anthracycline.Eur J Cancer 1996;32:47-5la.
23. Kampan NC, Madondo MT, McNally OM, Quinn M, Plebanski M. Paclitaxel and its evolving role in

the management of ovarian cancer. BioMed Res Int 2015; 2015: 1-

21http://dx.doi.org/10.1155/2015/413076 PMID: 26137480

24. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71(3): 209-49
25. Akerley W III. Paclitaxel in advanced non-small cell lung cancer : An alternative high-dose weekly schedule. Chest 2000; 117(4): 152S-5S.
26. Löwe J, Li H, Downing KH, Nogales E. Refined structure of αβ-Tubulin at 3.5 Å resolution edited by I. A. Wilson. J Mol Biol 2001; 313(5): 1045-57. http://dx.doi.org/10.1006/jmbi.2001.5077 PMID: 11700061
27. Zhang DY, Dmello C, Chen L, et al. Ultrasound-mediated delivery Of paclitaxel for glioma: A comparative study of distribution, toxIcity, and efficacy of albumin-bound versus Cremophor formulaTions. Clin Cancer Res 2020; 26(2): 477-86. http://dx.doi.org/10.1158/1078-0432.CCR-19-2182 PMID:31831565
28. Löwe J, Li H, Downing KH, Nogales E. Refined structure of αβ-Tubulin at 3.5 Å resolution edited by I. A. Wilson. J Mol Biol 2001; 313(5): 1045-57. http://dx.doi.org/10.1006/jmbi.2001.5077 PMID: 11700061
29. Urakami S, Igawa M, Kikuno N, et al. Combination chemotherapy With paclitaxel, estramustine and carboplatin for hormone refracto-Ry prostate cancer. J Urol 2002; 168(6): 2444-50. http://dx.doi.org/10.1016/S0022-5347(05)64164-X PMID: 12441936
30. Ma G, Liu Y, Peng C, Fang D, He B, Nie J. Paclitaxel loaded Electrospun porous nanofibers as mat potential application for Chemotherapy against prostate cancer. Carbohydr Polym 2011; 86(2): 505-12. http://dx.doi.org/10.1016/j.carbpol.2011.04.082
31. Benedetti Panici P, Palaia I, Graziano M, Bellati F, Manci N, Angioli R. Intraperitoneal paclitaxel as consolidation treatment in ovarian cancer patients: a case control study. Oncology 2010; 78(1): 20-5.

http://dx.doi.org/10.1159/000287968 PMID: 20185937

32. Bae JH, Lee JM, Ryu KS, et al. Treatment of ovarian cancer with paclitaxel- or carboplatin-based intraperitoneal hyperthermic chemotherapy during secondary surgery. Gynecol Oncol 2007; 106(1): 193- 200. http://dx.doi.org/10.1016/j.ygyno.2007.03.019 PMID: 17466362.
33. D.A. Yardley, nab-Paclitaxel mechanisms of action and delivery, J Control Release, 170 (2013) 365- 372.
34. A.C. Anselmo, S. Mitragotri, Nanoparticles in the clinic, Bioengineering & Translational Medicine, 1 (2016) 10-29.
35. V.P. Torchilin, Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery, Nature reviews. Drug discovery, 13 (2014) 813-827.
36. N.I. Marupudi, J.E. Han, K.W. Li, V.M. Renard, B.M. Tyler, H. Brem, Paclitaxel: a review of adverse toxicities and novel Delivery strategies, Expert Opin Drug Saf, 6 (2007) 609-621.
37. S.C. Kim, D.W. Kim, Y.H. Shim, J.S. Bang, H.S. Oh, S.W. Kim, M.H. Seo, In vivo evaluation of polymeric micellar paclitaxel formulation: toxicity and efficacy, Journal of Controlled Release, 72 (2001) 191-202.
38. H. Gelderblom, J. Verweij, K. Nooter, A. Sparreboom, Cremophor EL: the drawbacks and advantages

of vehicle selection For drug formulation, European journal of cancer, 37 (2001) 1590-1598.

39. A. Sparreboom, L. Van Zuylen, J. Verweij, K. Mross, E. Brouwer, L. Gianni, Interrelationships of paclitaxel disposition, Infusion duration and Cremophor EL kinetics in cancer patients., Clin Cancer Res, 5 (1999) 3840s-3840s.
40. W. Lorenz, H.J. Reimann, A. Schmal, P. Dormann, B. Schwarz, E. Neugebauer, A. Doenicke, Histamine-Release in Dogs by Cremophor-El and Its Derivatives – Oxethylated Oleic-Acid Is Most Effective Constituent, Agents Actions, 7 (1977) 63-67.
41. M.R. Green, G.M. Manikhas, S. Orlov, B. Afanasyev, A.M. Makhson, P. Bhar, M.J. Hawkins, Abraxane(®), a novel Cremophor(®)-free, albumin-bound particle form of paclitaxel for the treatment of advanced non-small-cell lung cancer, Ann Oncol, 17 (2006) 1263-1268.
42. W.J. Gradishar, Albumin-bound paclitaxel: a next-generation taxane, Expert Opin Pharmaco, 7 (2006) 1041-1053.
43. K. Paal, J. Muller, L. Hegedus, High affinity binding of paclitaxel to human serum albumin, Eur J Biochem, 268 (2001) 2187-2191.
44. W.J. Gradishar, S. Tjulandin, N. Davidson, H. Shaw, N. Desai, P. Bhar, M. Hawkins, J. O'Shaughnessy, Phase III trial of Nanoparticle albumin-bound paclitaxel compared with polyethylated castor oil-based paclitaxel in women with breast cancer, J Clin Oncol, 23 (2005) 7794-7803.
45. S. Singh, A.K. Dash, Paclitaxel in Cancer Treatment: Perspectives and Prospects of its Delivery Challenges, Crit Rev Ther Drug, 26 (2009) 333-372.
46. https://m.indiamart.com/proddetail/taxol-100-mg-injection-21409606033.html
47. https://m.indiamart.com/proddetail/abraxane-nab-paclitaxel-injection-16367577291.html
48. Q. Chen, Q.Z. Zhang, J. Liu, L.Q. Li, W.H. Zhao, Y.J. Wang, Q.H. Zhou, L. Li, [Multi-center prospective randomized trial on Paclitaxel liposome and traditional taxol in the treatment of breast cancer and non- small-cell lung cancer], Zhonghua zhong Liu za zhi [Chinese journal of oncology], 25 (2003) 190-192.
49. X. Xu, L. Wang, H.Q. Xu, X.E. Huang, Y.D. Qian, J. Xiang, Clinical Comparison between

Paclitaxel Liposome (Lipusu ®) And Paclitaxel for Treatment of Patients with Metastatic Gastric Cancer, Asian Pac J Cancer P, 14 (2013) 2591-2594.

50. T.Y. Kim, D.W. Kim, J.Y. Chung, S.G. Shin, S.C. Kim, D.S. Heo, N.K. Kim, Y.J. Bang, Phase I and pharmacokinetic study of Genexol-PM, a cremophor-free, polymeric micelle-formulated paclitaxel, in patients with advanced malignancies, Clin Cancer Res, 10 (2004) 3708-3716.
51. W.T. Lim, E.H. Tan, C.K. Toh, S.W. Hee, S.S. Leong, P.C. Ang, N.S. Wong, B. Chowbay, Phase I pharmacokinetic study of a Weekly liposomal paclitaxel formulation (Genexol-PM) in patients with solid tumors, Ann Oncol, 21 (2010) 382-388.
52. K.S. Lee, H.C. Chung, S.A. Im, Y.H. Park, C.S. Kim, S.B. Kim, S.Y. Rha, M.Y. Lee, J. Ro, Multicenter phase II trial of Genexol-PM, a Cremophor-free, polymeric micelle formulation of paclitaxel, in patients with metastatic breast cancer, Breast Cancer research and treatment, 108 (2008) 241-250.
53. M.W. Saif, N.A. Podoltsev, M.S. Rubin, J.A. Figueroa, M.Y. Lee, J. Kwon, E. Rowen, J. Yu, R.O. Kerr, Phase II clinical trial of Paclitaxel loaded polymeric micelle in patients with advanced pancreatic cancer,Cancer investigation, 28 (2010) 186-194
54. T. Boulikas, M. Vougiouka, Oncol. Rep. 10 (2003) 1663.
55. D.N. Church, A. Bahl, Cancer Treat. Rev. 32 (2006) 588.
56. S. Fu, J.J. Kavanagh, W. Hu, R.C. Bast, Int. J. Gynecol. Cancer 16 (2006) 1717.
57. H. Choy, Expert Rev. Anticancer Ther. 6 (2006) 973.
58. L.M. Pasetto, M.R. D0 Andrea, A.A. Brandes, E. Rossi, S. Monfardini, Crit. Rev. Oncol. Hematol. 60 (2006) 59.
59. R.J. Knox, F. Friedlos, D.A. Lydall, J.J. Roberts, Cancer Res. 46 (1986) 1972.
60. R.N. Bose, Mini. Rev. Med. Chem. 2 (2002) 103.
61. J.C. Dabrowiak, Metals in Medicine, Wiley, Chichester, UK, 2009.
62. R.A. Alderden, M.D. Hall, T.W. Hambley, J. Chem. Educ. 83 (2006) 728.
63. W.J.F. Van der Vijgh, Clin. Pharmacokinet. 21 (1991) 242.
64. https://en.m.wikipedia.org/wiki/File:Carboplatin-skeletal.svg
65. https://www.hopkinsmedicine.org/news/newsroom/news-releases/2019/03/new-drug-combination- shows-promise-for-common-pediatric-brain-tumor
66. Brazilian Journal of Pharmaceutical Sciences vol. 50, n. 4, oct./dec., 2014 http://dx.doi.org/10.1590/S1984-82502014000400004
67. D. S. Alberts, S. Green, E. V. Hannigan, R. O'Toole, D. Stock-Novack, P. Anderson,E. A. Surwit, V. K. Malvlya, W. A. Nahhas, C. J. Jolles, J. Clin. Oncol. 1992, 10, 706.
68. .K. Swenerton, J. Jeffrey, G. Stuart, M. Roy, G. Krepart, J. Carmichael, P. Drouin, R.Stanimir, G. O'Connell, G. MacLean, J. Clin. Oncol. 1992, 10, 718.
69. A. R. MacKenzie, Cancer 1966, 19, 1369.
70. D. J. Higby, H. J. Wallace, D. J. Albert, J. F. Holland, Cancer 1974, 33, 1219.
71. P. D. Bonomi, D. M. Finkelstein, J. C. Ruckdeschel, R. H. Blum, M. D. Green, B. MaSon, R. Hahn, D. C. Tormey, J. Harris, R. Comis, J. Clin. Oncol. 1989, 7, 1602.
72. C. Pallares, M. A. Izquierdo, A. Paredes, A. Fernandez Sagarra, L. De Andres, J. J. Lopez Lopez, Cancer 1991, 68, 40.
73. G. Calais, M. Alfonsi, E. Bardet, C. Sire, H. Bourgeois, C. Bergerot, B. Rhein, J. TorTochaux, P. Oudinot, P. Maillard, A.

Favre, P. H. Bertrand, Proc. Annu. Meet. Am. Soc.Clin. Oncol. 1998, 17, A1484.

74. J. Bourhis, J. P. Pignon, L. Designe, M. Luboinski, S. Guerin, C. Domenge, Proc. Annu. Meet. Am. Soc. Clin. Oncol. 1998, 17, A1486.
75. C. N. Sternberg, A. Yagoda, H. I. Scher, R. C. Watson, H. W. Herr, M. J. Morse, P. C.Sogani, E. D. Vaughan Jr., N. Bander, L. R. Weiselberg, J. Urol. 1988, 139, 461.
76. D. J. Vaughn, S. B. Malkowicz, B. Zoltick, R. Mick, P. Ramchandani, C. Holroyde, B.Armstead, K. Fox, A. Wein, J. Clin. Oncol. 1998, 16, 255.
77. Petrioli R, Frediani B, Manganelli A et al. Comparison between a cisplatin-containing regimen and a carboplatin-containing regimen for recurrent or metastatic bladder cancer patients. A randomized phase II study. Cancer 1996; 77(2): 344-51.
78. F. Panettiere, L. Leichman, E. Tilchen, T. T. Chen, Cancer Treat. Rep. 1984, 68, 1023,
79. M. Ravry , M. Moore, Clin. Oncol. 1980, 21, 353.
80. H. Bleiberg, T. Conroy, B. Paillot, A. J. Lacave, G. Blijham, J. H. Jacob, L. Bedenne,
81. W. P. McGuire III, J. Arseneau, J. A. Blessing, P. J. DiSaia, K. D. Hatch, F. T. Given Jr., N. N. Teng, W. T.Creasman, J. Clin. Oncol. 1989, 7, 1462.
82. https://m.indiamart.com/proddetail/carboplatin-injection-carboplatin-4654643333.html
83. https://tajlifesciences.com/portfolio/carboplatin-injection-bp-10mg-ml-450mg-45ml/
84. Journal of Applied Pharmaceutical Science,available online at www.japsonline.com Stability Testing of Pharmaceutical Products ,Sanjay Bajaj, Dinesh Singla and Neha Sakhuja.
85. Bardin C, Astier A, Vulto A, et al. Guidelines for the practical stability studies of anticancer drugs: a European consensus conference. Ann Pharm Franc¸ aises 2011; 69: 221–231.
86. Kaiser J and Kramer I. Long-term stability of clofarabineinjection concentrate and diluted clofarabine infusion solution. J Oncol Pharm Practice 2012; 18: 213–221.
87. Beignen JH. Home-based chemotherapy confronts pharmacist with stability and compatibility problems. Pharm Weekblad Sci Ed 1992; 14: 337.
88. Astier A. Compatibility of anticancer drug solutions With administering devices. EJHPP Pract 2008 ;14:55-56.

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