



STUDY ON THE DOCETAXEL AND ITS SIDE EFFECT

* Pankaj Kumar and **Dr. Dhirendra Babji Sanghai

¹Research Scholar, Department of Pharmacy, SunRise University, Alwar, Rajasthan (India)

²Professor, Department of Journalism and Pharmacy, SunRise University, Alwar, Rajasthan (India)

Email: pnkjpatel6@gmail.com

Abstract: One of the main concerns that oncologists have in the use of complementary and alternative medicine (CAM) is the possibility of the negative interactions of nutritional supplements with chemotherapy, causing reduced effectiveness of the cancer treatment. The purpose of this study was to search commonly used databases and look for actual research data (in vitro, in vivo, or human studies) that document any interactions (positive or negative) of nutritional supplements with docetaxel, a commonly used chemotherapeutic drug. The search revealed 24 articles that document interaction with docetaxel and certain nutritional supplements such as L-glutamine, fish oil, vitamin D, garlic, black cohosh, and others. Twenty-two of the studies documented some benefit in the combined use in terms of improving the apoptotic and cytotoxic effects of docetaxel on the tumors as well as reducing the toxicity and side effects involved in the use of docetaxel. From the current search, it seems as if more evidence supports the combined use of certain nutritional supplements with docetaxel in terms of beneficial effects. On the other hand, one needs to be cautious as well as certain supplements can have a negative effect, such as reducing the effectiveness of the drug. There is a dire need to further evaluate the negative and positive interactions of nutritional supplements and chemotherapeutic drugs.

[Kumar, P. and Sanghai, D.B. **STUDY ON THE DOCETAXEL AND ITS SIDE EFFECT**. *N Y Sci J* 2024;17(5):10-15]. ISSN 1554-0200 (print); ISSN 2375-723X (online). <http://www.sciencepub.net/newyork>. 02. doi:10.7537/marsnys170524.02.

Keywords: alternative medicine, cancer care, complementary medicine, docetaxel, herb–drug interaction, integrative medicine, integrative oncology, medicinal herbs, nutritional supplements

Introduction:

The National Center of Complementary and Alternative Medicine (<http://nccam.nih.gov/health/whatiscam>) defines “complementary and alternative medicine” (CAM) as a group of diverse medical and health care systems, practices, and products that are not generally considered to be part of conventional medicine. Recently, the use of CAM has increased considerably in the United States, and CAM is now being used for a variety of purposes, from back pain to adjuvant in cancer therapy. 1 The 2008 National Health Statistics report estimated that almost 4 of 10 adults (38.3%) used some type of CAM in the previous 12 months. 1 Nutritional supplements were the most frequently used CAM modalities (18% of those who used some kind of CAM), followed by deep-breathing exercises (13%). 1 CAM is increasingly being used by cancer patients in conjunction with their cancer therapy. Estimating the number of cancer patients who use CAM is difficult because studies show varied results. Reported CAM use ranges from 30% in some studies to 83% in others, averaging around 50%, which is much higher than CAM use in the general population. 2,3 Use of CAM also varies by the type of cancer, with

the highest use among breast cancer patients (approximately 86%), 4 followed by patients with brain tumors (approximately 30%). 5 The majority of cancer patients who use CAM do so to boost their immune systems. CAM is also used to improve patients’ quality of life, avert treatment drugs’ side effects, improve cancer-related symptoms, and prevent cancer recurrence; CAM is also used for its direct anticancer effects. 6 It is also believed to be beneficial in helping patients cope with pain, distress, negative emotions, and anxiety. More and more patients are combining CAM with their conventional medications, but the majority do not discuss CAM use with their physicians. It is estimated that 38 to 60% of cancer patients participate in CAM practices without informing their attending physicians. 2 A recent survey revealed that 36 to 64% of physicians estimated that less than 25% of their patients used CAM, whereas 34% of the patients said they did so. 7 Many physicians admit they are concerned about the pharmacodynamic interactions between prescribed treatment drugs and supplements that patients use. This is highlighted by a study in which 84% of attending physicians thought they needed to learn more about CAM to sufficiently address patients’

concerns. 8 Another study showed that 24% of primary care physicians never referred patients to complementary medicine physicians, 69% did so occasionally, and 70% admitted they had little or no knowledge of herbal remedies. 9 Physicians are understandably worried about the safety of their patients and thus do not recommend any CAM therapies about which they are not very sure. The lack of knowledge about CAM among conventional physicians is compounded by uncertainty about how CAM therapies and conventional chemotherapies interact. Some authorities have expressed concern about the use of CAM with chemotherapy because of the potential risk for negative interactions between the two. Thus, many attending physicians are limited in their ability to effectively treat their patients not only because they are unaware of the possible interactions between conventional drugs and the dietary supplements used in CAM but also because they are unaware of their patients' CAM use because patients are hesitant to discuss CAM with their attending physicians. 10,11 Data on the potential interactions between the majority of the herbal supplements and chemotherapeutic drugs have been inconsistent. Numerous recommendations have been deduced theoretically on the basis of the potential influence of herbs on the metabolism of the drugs, which affects the drug's pharmacokinetic and pharmacodynamic properties. Herbs can alter all aspects of a drug's pharmacokinetics, including absorption (by altering the absorption rate), distribution (by causing protein-binding displacement), metabolism (by affecting the CYP enzymes), and excretion. 12 The most important and widely accepted interaction is the alteration of a drug's metabolism by affecting the CYP enzymes. 13,14 This class of enzymes is responsible for the metabolism of drugs in the human body, so any increase or decrease in activity may lead to failure of the therapy or increased toxicity. Most clinicians raise a concern about the potential interaction that herbs might have with conventional drugs. Garlic, a common dietary supplement, has been said to affect several CYP enzymes (CYP2C9, CYP2C19, CYP3A4, CYP3A5, and CYP3A7) and thus may interfere with the action of various drugs that are also metabolized along the CYP pathway, such as docetaxel, etoposide, imatinib mesylate, irinotecan, and paclitaxel, and may cause partial metabolism of other drugs, such as cyclophosphamide, ifosfamide, tamoxifen, vinblastine, and vincristine. 15 The same concern is present for other herbs, including Echinacea angustifolia, ginkgo, ginseng, grapeseed, grapefruit juice and peel, and soy, which are also thought to affect the CYP3A4 enzyme and thus might affect the metabolism of these chemotherapy drugs. 12 Because of this, more caution is necessary when considering

the combination of these herbs and drugs. Likewise, Sparreboom and colleagues have expressed concern over combining chemotherapy drugs, especially taxanes, with certain herbs, such as echinacea, St. John's wort, kava, and grapeseed. 12 We chose to focus on one chemotherapeutic drug, docetaxel, which is commonly used for breast cancer, ovarian cancer, lung cancer, and other malignancies. In this study, we searched for evidence of interactions between docetaxel and nutritional supplements. We looked for either positive or negative interactions. We felt that searching the interactions with this commonly used chemotherapeutic drug as an example could help in clarifying the combined use of nutritional supplements and chemotherapy in terms of harm or benefit.

Docetaxel works by disrupting the microtubular network in cells, which is essential for cell division and other normal cellular functions. Docetaxel interferes with the function of microtubules, resulting in inactive microtubule bundles, causing cells to die.

How to Take Docetaxel

Docetaxel is given by intravenous (IV, into a vein) infusion, usually over an hour. The dosage and schedule are determined by the person's size and type of cancer. It can be given alone or with other drugs. You will be given a corticosteroid prior to the infusion to prevent severe fluid retention and allergic reactions. The steroid is given in pill form or by IV, which will be determined by your healthcare provider.

This medication contains alcohol and may cause intoxication. You should not drive after the infusion until you know how it will affect you.

Grapefruit can change how your body absorbs this medication. Do not eat grapefruit or drink grapefruit juice during the 2 days before, the day of, and two days after each dose.

This medication can cause severe side effects if given to a patient whose liver function is abnormal. Your labs will be closely monitored prior to each dose of docetaxel and the dose may be decreased or held if your liver function is not normal.

Even when carefully and correctly administered by trained personnel, this drug may cause a feeling of burning and pain. There is a risk that this medication may leak out of the vein at the injection site, resulting in tissue damage that can be severe. If the area of injection becomes red, swollen, or painful at any time during or after the injection, notify your care team immediately. Do not apply anything to the site unless instructed by your care team.

Possible Side Effects of Docetaxel

There are a number of things you can do to manage the side effects of docetaxel. Talk to your care team about these recommendations. They can help you decide

what will work best for you. These are some of the most common or important side effects:

Allergic Reactions

Allergic reactions are possible with this medication. Signs of a reaction can include: shortness of breath or difficulty breathing, swelling of the face, lips, tongue or throat, trouble swallowing, chest pain, rash, flushing, hives or itching, or a decrease in blood pressure. If you notice any changes in how you feel during the infusion, let your nurse know immediately. The infusion will be slowed or stopped if this occurs.

Fluid Retention

Docetaxel can cause your body to hold too much fluid, which can be a serious side effect. Medications will be given before each treatment to decrease the risk of this side effect. Call your healthcare provider if you do not urinate for more than 12 hours, experience shortness of breath, have an unexpected weight gain, or develop swelling in your hands, feet, ankles or legs.

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F /38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever, or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your doctor or nurse know if you experience any shortness of breath, difficulty breathing, or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums, or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib), etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding the use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become thin, brittle, or may fall out. This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats, and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold weather or to protect you from the sun.

Fatigue

Fatigue is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

Peripheral Neuropathy (Numbness or Tingling in the Hands and/or Feet)

Peripheral neuropathy is a toxicity that affects the nerves. It causes numbness or a tingling feeling in the hands and/or feet, often in the pattern of a stocking or glove. This can get progressively worse with additional doses of the medication. In some people, the symptoms slowly resolve after the medication is stopped, but for some, it never goes away completely. You should let the oncology care team know if you experience numbness or tingling in the hands and/or feet, as they may need to adjust the doses of your medication.

Nail and Skin Changes

Your fingernails/toenails may become dark, brittle or fall off. You may notice dry skin or changes in the color or tone of your skin. Your skin will be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is completed. Avoid the sun between 10-2 pm, when it is strongest. Wear sunscreen (at least SPF 15) every day, wear sunglasses and long sleeves/pants to protect your skin. Keep your fingernails and toenails clean and dry. You may use nail polish, but do not wear fake nails. If any nails fall off, clean the nail bed well with soap and water and cover with a Band-Aid.

Mouth Ulcers (Mucositis)

Certain cancer treatments can cause sores or soreness in your mouth and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek or throat becomes white, ulcerated, or painful. Performing regular mouth care can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages, and citrus juices.

Diarrhea

Your oncology care team can recommend medications to relieve diarrhea. Also, try eating low-fiber, bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain bread, cereals, and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve

diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, un-caffeinated fluid a day to prevent dehydration.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy, or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Constipation

There are several things you can do to prevent or relieve constipation. Include fiber in your diet (fruits and vegetables), drink 8-10 glasses of non-alcoholic fluids a day, and keep active. A stool softener once or twice a day may prevent constipation. If you do not have a bowel movement for 2-3 days, you should contact your healthcare team for suggestions to relieve constipation.

Decrease in Appetite or Taste Changes

Nutrition is an important part of your care. Cancer treatment can affect your appetite and, in some cases, the side effects of treatment can make eating difficult. Ask your oncology care team about nutritional counseling services at your treatment center to help with food choices.

- Try to eat five or six small meals or snacks throughout the day, instead of 3 larger meals.
- If you are not eating enough, nutritional supplements may help.
- You may experience a metallic taste or find that food has no taste at all. You may dislike foods or beverages that you liked before receiving cancer treatment. These symptoms can last for several months or longer after treatment ends.
- Avoid any food that you think smells or tastes bad. If red meat is a problem, eat chicken, turkey, eggs, dairy products, and fish without a strong smell. Sometimes cold food has less of an odor.
- Add extra flavor to meat or fish by marinating it in sweet juices, sweet and sour sauce, or dressings. Use seasonings like basil, oregano, or rosemary to add flavor. Bacon, ham, and onion can add flavor to vegetables.

Muscle or Joint Pain/Aches

Your healthcare provider can recommend medications and other strategies to help relieve pain.

Less common, but important side effects can include:

- **Radiation Recall:** Radiation recall is when the administration of a medication causes a skin reaction that looks like a sunburn (redness, swelling, soreness, peeling skin) in areas where radiation was previously given. Notify your oncology team if you notice this side effect. Treatment can include topical steroid ointments and a delay in your next chemotherapy dose.
- **Vision Problems:** Docetaxel can cause eye problems that cause blurred vision or loss of vision. Report any vision changes to your healthcare team immediately.
- **Secondary Cancers:** A secondary cancer is one that develops as a result of cancer treatment for another cancer. This is quite rare, but you should be aware of the risk. In most cases, a secondary cancer related to chemotherapy is a blood cancer (leukemia, lymphoma, myelodysplastic syndrome, renal cancer). This can occur years after treatment. This is most often associated with repeated treatments or high doses. Your provider will monitor your labs closely. Consider having a complete blood count with differential checked annually by your healthcare provider if you received high risk therapies.
- **Skin Reactions:** This medication can cause a skin reaction that progresses from redness with swelling to peeling skin. Be sure to inform your provider of any skin changes you develop as skin reactions can become serious.
- **Neurologic Reactions:** This medication can cause abnormal burning or prickling sensations (paresthesia), abnormal sense of touch (dysesthesia), and pain. If you are having any of these symptoms, contact your care team.
- **Neutropenic enterocolitis/Typhlitis/Colitis:** Docetaxel can cause bowel problems that can be very serious. Notify your care team immediately if you experience stomach pain with or without a fever, tenderness in your stomach, or diarrhea.
- **Tumor Lysis Syndrome:** If there are a large number of tumor cells in your body

prior to treatment, you are at risk for tumor lysis syndrome. This happens when the tumor cells die too quickly and their waste overwhelms the body. You may be given medication (allopurinol) and IV fluids to help prevent this. If you experience nausea, vomiting, diarrhea, or become lethargic (drowsy, sluggish), notify your oncology team right away. TLS can affect your kidney function. Your provider will monitor your kidney function with blood work. Notify your provider if you have little or no urine output.

References

- [1]. Barnes PM, Bloom B, Nahin RL. Complementary and alternative medicine use among adults and children: United States, 2007. National Health Statistics Report 2008; Number 12. US Dept of Health and Human Services, Centers for Disease Control and Prevention. Natl Health Stat Report 2008; (12): 1–23.
- [2]. Richardson MA, Sanders T, Palmer JL, et al. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *J Clin Oncol* 2000; 18: 2505–14.
- [3]. Ernst E, Cassileth BR. The prevalence of complementary/alternative medicine in cancer: a systematic review. *Cancer* 1998; 83: 777–82.
- [4]. Greenlee H, Kwan ML, Ergas IJ, et al. Complementary and alternative therapy use before and after breast cancer diagnosis: the Pathways Study. *Breast Cancer Res Treat* 2009;117:653–65. [Epub 2009 Jan 31]
- [5]. Armstrong TS, Gilbert MR. Use of complementary and alternative medical therapy by patients with primary brain tumors. *Curr Neurol Neurosci Rep* 2008; 8: 264–8.
- [6]. Humpel N, Jones SC. Gaining insight into the what, why, and where of complementary and alternative medicine use by cancer patients and survivors. *Eur J Cancer Care (Engl)* 2006; 15: 362–8.
- [7]. Joyce E, Gallagher J, Tenhover J, et al. Complementary therapies: knowledge, attitudes and use among providers. Poster presented at Association of Oncology Social Workers Annual Conference; 2004; Washington, DC.
- [8]. Winslow LC, Shapiro H. Physicians want education about complementary and alternative medicine to enhance communication with their patients. *Arch Intern Med* 2002; 162: 1176–81.
- [9]. Givon SM, Liberman N, Klang S, et al. A survey of primary care physicians' perceptions of their

patients' use of complementary medicine. *Complement Ther Med* 2003; 11: 254– 60.

- [10]. Navo MA, Phan J, Vaughan C, et al. An assessment of the utilization of complementary and alternative medication in women with gynecologic or breast malignancies. *J Clin Oncol* 2004; 22: 671– 7.

4/21/2024