NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

Saving Trees to Save Cancer Patients

by

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Part I – Saving Patients

You are a newly hired researcher for All About Yew Therapeutics. You are excited to apply your knowledge and skills towards fighting cancer. The first task you are assigned is to save a specific tree species. But wait! How does that relate to cancer therapy? Thankfully, your cheerful and helpful friend (your instructor), is going to share with you a PowerPoint presentation to help you understand the significance of phytochemicals and why they are significant in the realm of anticancer therapies.

Background

All About Yew Therapeutics's foundation was inspired by the discovery of a compound found in nature by Dr. Arthur Barclay in 1962 called "taxol" (now known by its scientific name as "paclitaxel"). Little did he know that this compound, originally derived from the bark of the Pacific yew tree (*Taxus brevifolia*), possessed properties that could stop cells from dividing. But how could this be? Researchers, including Monroe Wall and Mansukh Wani, were able to determine the highly complex structure of paclitaxel, which coincides with its unique mechanism of action. Paclitaxel's structure allows it to bind allosterically to microtubule components, preventing microtubule depolymerization and cell replication. Clinical studies have also shown paclitaxel's ability to cause considerable regression in certain models of tumors.

Discoveries in nature, such as paclitaxel's discovery, provide a new perspective for anticancer drug treatment. Insight into paclitaxel's complex structure can aid researchers in the synthesis of other forms of anticancer drugs. This is particularly significant because nature's supply is finite, and with the Pacific yew trees' extremely low yield for paclitaxel, there is urgency in finding alternatives. Therefore, it is important to thoroughly understand paclitaxel, and in the meantime, investigate efficient methods in which the Pacific yew tree population can be maintained.

It's up to you and your coworkers to take on this important task. Good luck and listen carefully to your friend as they go over the PowerPoint slides; they will help you to answer the questions below.

Questions

1. What are traditionally synthesized anti-cancer drugs? Your answer should include the general function of these drugs and some limitations of traditionally synthesized drugs.

2. Plants produce phytochemicals that can be used to resolve a variety of human illnesses. In cancer treatment they are able to function as plant-derived anticancer drugs. Why might phytochemicals be a potential alternative for cancer treatment?

3. Fill in Table 1 below comparing traditionally synthesized drugs (TSD) with plant-derived drugs (PDD).

   Table 1. Comparison of traditionally synthesized drugs with plant-derived drugs.

	TSD	*PDD*
Supply		
Cost		
Selectivity and side effects		

4. Which type of drug do you think has more potential in cancer treatment, based on each drug's efficacy, side effects, toxicity, source, cost, etc.?

5. Paclitaxel is a plant-derived drug from yew trees. It is produced in the trees as a plant immunity compound against wood-degrading fungi. What is paclitaxel's mechanism of action against fungi?

Wow! Phytochemicals like paclitaxel seem like a solid alternative to traditionally synthesized drugs. But how exactly does paclitaxel work to fight cancer? Your friend insists that you research more on the mechanism; it's important to understand the enemy in order to win against it! Good thing you have a research team with you to learn more about paclitaxel.

6. Paclitaxel's mechanism of action in human cancer cells also targets microtubules. Read the following article to help you answer the questions further below:
   - Arnal, I & R.H. Wade. (1995). How does taxol stabilize microtubules? *Current Biology* 5(8): 900–8. <https://doi.org/10.1016/s0960-9822(95)00180-1>

   a. Draw a labeled diagram showing the basic structure of microtubules, as described in the background section of the article. Make sure you clearly include heterodimers and protofilaments.

   b. According to the background section of the article, what is paclitaxel's effect on microtubule assembly? Include the following terms in your explanation: *critical concentration, polymerization rate,* and *stabilization*. How does this relate to paclitaxel's role in cancer treatment?

   c. According to Figure 8 of the artice, how does the conformational change of the tubulin dimers affect microtubule stabilization in the presence of paclitaxel? (You may draw diagrams with labels to aid your explanations.) Why is this significant to cancer therapy in the context of the cell cycle?

7. How does paclitaxel's mechanism of action against fungi compare to its use against human cancer cells? What is similar and what is different?

8. Why would paclitaxel's impact on microtubule assembly cause it to be an effective cancer treatment? (*Hint:* how does this relate to cell cycle disruption and apoptosis?)

Good work! Our next task is to figure out how we can actually save Pacific yew trees by using all the knowledge we just learned. You should now have a strong understanding of phytochemicals like paclitaxel and how they combat cancer cells. Now you know why it's so important to save the yew tree population!

Part II – Saving Trees

So far you've learned about phytochemicals and how paclitaxel can be used to combat cancer cells. Now that you understand the importance of paclitaxel, let's learn more about the issues revolving around the extraction of paclitaxel from yew trees. Next you are going to a watch a brief segment (the first 2:05 minutes only) of the following video to help you answer Question 9 below.

- *Saving the Cancer-Treating Maire's Yew Tree in Nepal.* Produced by Greenhood Nepal, 2020. YouTube. <https://youtu.be/EeDWxQ1kCAY>

Question

9. Paclitaxel is well known to be very costly due to its low yield: around three to ten trees are used for one patient. From watching the video clip, what are some major impacts of paclitaxel extraction on the yew population?

Seems like the yew trees do need a little hand! You want to develop some hypothetical solutions to help this tree species. You learn that there are many diverse approaches in developing a solution and you decide to refer to some primary research papers for help.

Question

10. Develop and present a strategy to hypothetically solve the shortage of paclitaxel without negatively impacting the Pacific yew tree abundance. Locate and select a primary research article in any of the four topics below to help you create your solution (~300 words).
    - Conservation management (e.g., ecological guidelines or regulations to protect the species).
    - Finding alternative sources (e.g., finding phytochemicals with similar characteristics or with similar structure and function as paclitaxel).
    - Genetic alterations (e.g., modifying the genome of yew trees).
    - Biotechnology (e.g., increased production of bioactive compounds in phytochemicals in a lab setting).

    Make sure to include:
    - A summary of your chosen article's purpose or goal, results, and conclusion.
    - An explanation of how the methods used in the article can also be utilized to help the yew tree population.
    - Two or three specific ideas from the article.

Your friend really likes your solution for saving the yew trees and they went ahead and proposed your idea to the head of the corporation. Hopefully, with your help and solution, the yew population can become stable in no time, and paclitaxel can be more widely available in cancer treatment!