PHYSICAL SCIENCE JOURNAL FOR TEENS

SEPTEMBER 2021

How can we make antimalarial medicine faster?

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Abstract

For most people, getting a mosquito bite is annoying. For others, it could be life-threatening. Mosquitoes are carriers of many diseases, including malaria. According to the World Health Organization, in 2019 there were 229 million cases of malaria worldwide and about 409,000 people died from this disease. This is why scientists are trying to make the antimalarial medicine artemisinin more available.

Artemisinin forms from dihydroartemisinic acid (DHAA). In this study, we collected data to see how heat and light affect how fast artemisinin forms from DHAA. We also looked at how the amount and chemical composition of DHAA affect the formation of artemisinin. Our data support the need for an optimal amount of ultraviolet light to produce artemisinin faster. We also discovered that the presence of hydrogen isotopes (deuteriums) on DHAA slows down the process of forming artemisinin. But increasing the amount of DHAA can significantly increase artemisinin production.

Introduction

Every two minutes, a child dies from **malaria**. People all over the world are working to stop this disease. Malaria is caused by a parasite spread by mosquitoes. To stop malaria, we need to control mosquito populations and produce medications that can kill the parasite that causes this disease.

A natural medicine against malaria is artemisinin. It comes from a plant named *Artemisia annua*. This plant takes a chemical called dihydroartemisinic acid (DHAA) and turns it into artemisinin. Researchers are using chemistry to figure out how DHAA transforms into artemisinin so that we can make this **antimalarial** faster and in larger amounts.

In this study, we wanted to find out which factors affect how fast artemisinin forms. Could heat, light, the amount of DHAA, or the chemical composition of DHAA hold the key?

Sunlight helps *Artemisia annua* naturally make artemisinin, an antimalarial medicine.

Photo: Francis K. Yoshimoto

Methods

Experiment 1:

We placed samples of DHAA under an **infrared** light, in a bath of hot oil, and under an **ultraviolet light** (UV). The samples remained in their environments for 2.5 hours. We also put a sample of artemisinin under the UV lamp for 8 days to see how UV light can affect artemisinin. Then we measured the amount of artemisinin present in each sample using a **nuclear magnetic resonance (NMR) spectrometer** and a **mass spectrometer**.

For our next two sets of experiments, we created a form of DHAA in the lab that contains three **deuterium** atoms (Fig. 1). Deuterium is an **isotope** of hydrogen. The most common form of hydrogen (H) has one proton and no neutrons. Deuterium (D) has one proton and one neutron, so it is heavier than hydrogen.

An isotope is an atom that has the same number of protons as other atoms of the element, but it has a different number of neutrons. Think about an apple, which may look the same as another apple on the outside but has a different number of seeds on the inside.

Experiment 2:

We tested how fast DHAA with deuterium converted to artemisinin in a dark room, by a window, and under a UV lamp. We used a set of samples with 100 micrograms of DHAA and a set with only 10 micrograms of DHAA.

Experiment 3:

We mixed DHAA with and without deuteriums in a 1 to 1 ratio, then we looked for artemisinin using a mass spectrometer. By mixing the two forms of DHAA, we can directly compare how fast DHAA turns into artemisinin when it has deuterium and when it doesn't.

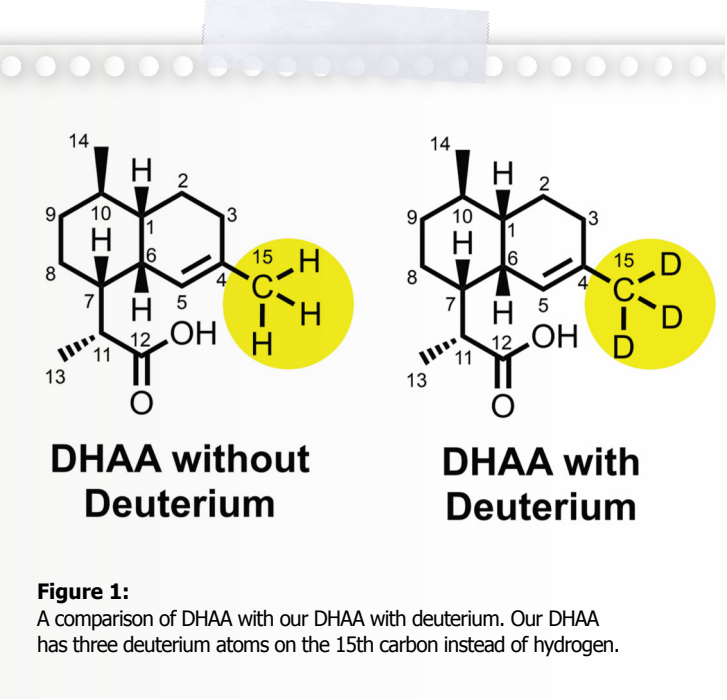

Figure 1:
A comparison of DHAA with our DHAA with deuterium. Our DHAA has three deuterium atoms on the 15th carbon instead of hydrogen.

Results

Experiment 1:

The UV light sample showed a larger amount of artemisinin compared to the infrared and hot bath samples. But when artemisinin was left under UV light for 8 days, the amount of artemisinin started to decrease. Instead, we found a chemical that had all the atoms of artemisinin, but in a different arrangement that does not kill the parasite that causes malaria.

Experiment 2:

In the first 24 hours, our DHAA with deuterium formed artemisinin 3.3 times faster in the light and 49 times faster under the UV light. However, at 120 and 312 hours, the rates of formation were about the same in the dark samples and the natural light samples. Under the UV light at 120 and 312 hours, the amount of artemisinin was 5.9 times and 50 times less compared to the dark. (See Table 1.) There was less artemisinin because the chemical with a different arrangement was forming.

We also learned that the amount of DHAA affects how much artemisinin forms. When we used 100 micrograms and 10 micrograms, we found that the vials with 100 micrograms made 39 times more artemisinin.

Experiment 3:

Artemisinin formation was faster for the DHAA without deuterium.

Please see Table 1 on Page 3

	Artemisinin Rate Comparison (How many times faster artemisinin is produced compared to dark)		
	Dark	Natural Light	UV Light
24 hours	1	3.3	49
47 hours	1	3.5	28
120 hours	1	1.2	0.17
320 hours	1	1.1	0.02

Table 1:
Results of the 100 microgram deuterium samples in the dark, natural light, and UV lamp over time.

What happens to the rate of artemisinin formation over time for the natural light and UV samples?

Discussion

Our results show that we need large amounts of DHAA and an optimal amount of UV light to produce the greatest amount of artemisinin. That is, we need enough but not too much in order to get the maximum amount of artemisinin as quickly as possible. You can probably think of some things in your life that work like that – for example, you need to eat enough food at lunch but not too much in order to have energy for your afternoon classes (but not fall asleep!).

Artemisinin forms faster in UV light than natural light, while heat doesn't help at all. But if the DHAA is under UV light for too long, it forms a new product that doesn't have antimalarial properties. Also, 10 times more DHAA created 39 times more artemisinin.

We also found out that artemisinin formation was faster for the DHAA without deuterium. You might think that means we wasted our time making the isotope with deuterium, but actually, it's always useful to find out what we shouldn't bother doing in the future!

Conclusion

Scientists are working hard to make treatments for malaria available at a low cost. You can help through donations to organizations such as Nothing but Nets. They send mosquito nets to countries in need.

Make sure to protect yourself from mosquitoes too! Wear long sleeves and pants and/or use insect repellent when you are in areas with mosquitoes. Also make sure doors and windows close properly so they can't get into your home. Even if you don't have to worry about malaria, there are other diseases mosquitoes can carry.

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Glossary of Key Terms

Antimalarial – a chemical that kills the parasite that causes malaria.

Deuterium – an isotope of hydrogen that has 1 proton and 1 neutron in the nucleus. The most common type of hydrogen, also known as protium, has 1 proton and 0 neutrons.

Infrared – electromagnetic energy that has a longer wavelength than visible light. The longer wavelength has a lower energy. This form of electromagnetic energy is used in heat sensors and night vision goggles.

Isotope – atoms of the same element that have the same number of protons and electrons, but have a different number of neutrons. For example, carbon-12 and carbon-14 are isotopes of carbon. They both have six protons and six electrons, but carbon-12 has 6 neutrons while carbon-14 has 8 neutrons.

Malaria – a blood disease transmitted by the bite of infected mosquitoes. Symptoms include fever, chills, muscle aches, headaches, and tiredness.

Mass spectrometer – a device used to identify the presence of chemical compounds. A mass spectrometer makes the compounds into an ion by removing electrons. Then they are moved through a magnetic field which exerts a force on them, causing them to move in a more circular path. The path they take depends on their mass. The mass spectrometer uses their path to identify what compound they are. Think about it like this: if you shoot water at a tennis ball flying by, then at a bowling ball, they'll end up in different places because they have differing masses.

Nuclear magnetic resonance (NMR) spectrometer – an instrument used to analyze the nuclei of compounds. The NMR spectrometer applies a magnetic field to samples containing compound(s) that have certain nuclei. Depending on the chemical environment of the nuclei, different signals are present.

Ultraviolet – electromagnetic energy that has a shorter wavelength than visible light. The shorter wavelength has higher energy. This form of electromagnetic energy is responsible for sunburns and suntans.

Check your understanding

1. Why do scientists want to use chemistry to make artemisinin?
2. Why did we conclude that there is an optimal amount of ultraviolet light exposure for making artemisinin from DHAA?
3. Based on our results, is it a good idea to use deuterium-containing DHAA to produce artemisinin? Why or why not?
4. Isotopes were used in this study to change the composition of the DHAA. Research some other ways that isotopes are used in our everyday lives. Give at least two examples.

Acknowledgment: This article's adaptation was supported by the Bill and Melinda Gates Foundation. BILL & MELINDA GATES foundation