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INTERVIEW

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Plants Go to War: A Botanical History of World War II

An Interview with Judith Sumner, PhD

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Dr. Judith Sumner is a botanist who has studied the genus *Pittosporum* extensively in the Pacific. She has a particular interest in ethnobotany and medicinal plants and has taught and lectured for several years at the Arnold Arboretum of Harvard University. Her first book, *The Natural History of Medicinal Plants*, was published by Timber Press (2000); it was followed by *American Household Botany: A History of Useful Plants, 1620-1900* (2004).

Judith has been awarded the Foster Award for Excellence in Herbal Literature from the Herb Society of America, and *American Household Botany* earned the American Horticultural Society Book Award in 2005.

Her newest book *Plants Go to War: A Botanical History of World War II,* McFarland and Company (2019), details the complex and intertwined history of WWII as it relates to medicinal botany and diverse other plant uses during the war years. Like a vine, it appears that medicinal plants had reached all areas of WWII, from Pacific to European theaters, so quietly and calmly that many of us have forgotten (or never learned) about the significant role they played. Quinine is likely the first and possibly only plant-based drug that comes to mind, but this book (and Chapter 7 in particular) effectively goes through the assortment of medicinal plants, their roles in wartime choices for conquest, and how this drove chemical synthesis that makes up most of our drugs released today. This is potentially a reference book, so every topic is covered in just enough interesting and often unexpected information to spur a self-motivated, in-depth *Wikipedia* search to understand the aforementioned plants and medicinal derivatives. Since WWII, much of the original need for medicinal plants has been eclipsed by synthetic drugs and patentable compounds. However, as Dr. Sumner describes in our interview, there might be a very real medicinal need for botanical drugs again in the future.

Can you describe how you first became interested in botany in general, and then more recently, medical botany?

I grew up outside of Boston and would describe my childhood as "free-range". We lived on a lake and nearby were farms. I knew all the farmers, and I was allowed to wander fairly far from home. I learned about plants and agricultural plants from a really young age. There were also remnants of colonial area medicinal plant gardens in the area around where we lived. We had a neighbor who started a phenomenal garden that ran behind all of our houses, so I spent time in the garden and listening to him

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talk about gardening in Italy. I spent a lot of time alone outside and that's how you might become a botanist. As a graduate student, I did field work in the Pacific region, and the genus I studied had numerous medicinal properties. As a botanist, I began teaching medicinal botany at the Arnold Arboretum of Harvard University. Ethnobotany is a significant part of medicinal botany and understanding how local people have discovered and used plants ties together the selection, uses, chemistry, and medicinal potential of many plant species.

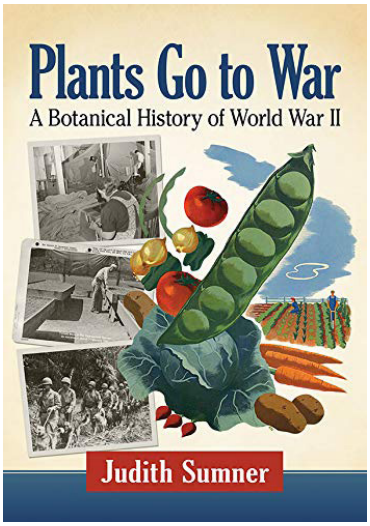
What inspired you to focus on the botanical history of WWII for this book?

Certainly, as an author, I'm looking for a book that hasn't been written; an original topic. It had been in my mind for at least a decade. My father was a doctoral student in chemistry during WWII and so enlisted as a chemist with the 43rd Chemical Laboratory Company. He shipped out to the island of Oahu to look into Japanese chemical and biological weapons. He was also involved in agar, rubber, food testing, and textiles; I realized almost everything he dealt with came from a plant. Then when I trained in the Pacific region, I was aware that the war had affected many of the atolls. For instance, before the war, native species grew in the Fiji Islands, but after kudzu was introduced by the US Army as a camouflage plant, it overran and out-competed much of the native Fijian vegetation. I was aware of the effect of the war, how plant products were used, and this all came together to looking at the war from a botanical perspective. Richard Evans Schultes, who is widely regarded as the father of modern ethnobotany, often said that botanists should be allowed to write history. *Plants Go to War: A Botanical History of World War II* is my way of following his instructions!

A number of these important discoveries are described as serendipitous, such as the discovery of penicillin and mauve color dye (a failed quinine synthesis attempt led to the discovery of mauve color dye). At the same time, many of the medicinal plants used in WWII were well known throughout history as providing relief for certain ailments. Can you discuss more about the roles of both serendipity and re-exploration of known medicinal plants in drug development?

Certainly, war moves medicine forward because there are special needs during war times, for instance gas gangrene that was caused by the soil bacterium *Clostridium perfringens*. Combat wounds could result in gas gangrene, which prior to WWII often resulted in amputations. Going into the war, penicillin was known as a potential antibiotic but not grown on an industrial scale.

Judith Sumner, PhD



Plants Go to War: A Botanical History of World War II, McFarland and Company (2019) by Judith Sumner.

The war resulted in the development of penicillin as a pharmaceutical drug; American microbiologists figured out how to culture the fungus on a corn-based medium. Another example involves malaria, which was a problem in both the southern US and in the Pacific. Quinine was known as an ethnobotanical drug since ancient times, since it both cures and prevents infections. The issue was that it was obtained from fever bark trees in Indonesia, an area under Japanese control. By the 1940s it was an ingredient in many drugs, so pharmacists were asked to turn in their quinine supplies for military use. The need for a quinine alternative is when serendipity comes in. Coal tar (derived from fossilized plants) was used to synthesize a wide range of organic compounds including dyes and the related compound atabrine, which had anti-protozoal activity and was a viable substitute for quinine. The prob-

lem is that atabrine has side-effects including yellowing skin and stomach discomfort, but it saved many lives during the war. Japanese propagandists were even telling American soldiers that atabrine caused impotence!

On the home front, there was concern about drug shortages, especially because drugs were expected to supply troops before civilian needs. The Massachusetts College of Pharmacy partnered with the Arnold Arboretum to plant two acres that looked very much like a colonial herb garden. The goal was to determine what would grow reliably in a New England climate and if necessary, provide medicinal alternatives in a time of need.

War, and the mere threat of war, seemed to be a strong factor in pushing new innovations in drug development and search for medicinal compounds from natural sources? Do you believe this is still true for countries or have scientists and funding bodies lost interest in searching the natural environment for new medicinal compounds?

If you look at big pharma, we don't see much investigation of natural products, possibly because it's difficult for them to own or patent a natural compound like those from plants [there are precedents in the US for prohibiting patents on "abstract ideas," "laws of natures," "natural products," and "natural phenomena"]. We estimate that only 10% of plant species in the world are known chemically. That's where ethnobotany comes in, if for no other reason just to retain local cultures and practical knowledge. If anything sends us back to the plant kingdom, it's going to be the need for antibiotics. The individual compounds from plants aren't going to be as effective as broad-spectrum antibiotics, but if you combine a variety of plant compounds, phytochemicals could provide effective broad-spectrum antibiotics. In fact, one of the most interesting ways to learn about potential antibiotic drugs is to look at herbarium specimens (Figure 1). Herbarium specimens are dried plants, typically mounted on acid free paper, that include detailed local information and even ethnobotanical lore. These notes on cultural uses could suggest potential antibiotic applications. Some families with known antibiotic uses are the mustards (Brassicaceae) and the mints (Lamiaceae); other families such as the nightshades (Solanaceae, which includes mandrake and belladonna) produce known analgesics. I don't think we're quite at the point of necessity, but I think that we will see a day when big pharmaceutical companies return to the botanical roots of medicine.

Many countries strategically seized lands that were integral to medicinal plant production. Could you talk more about this? In particular, you mention Japan and Germany invading countries in the Pacific that were able to grow trees necessary for quinine production.

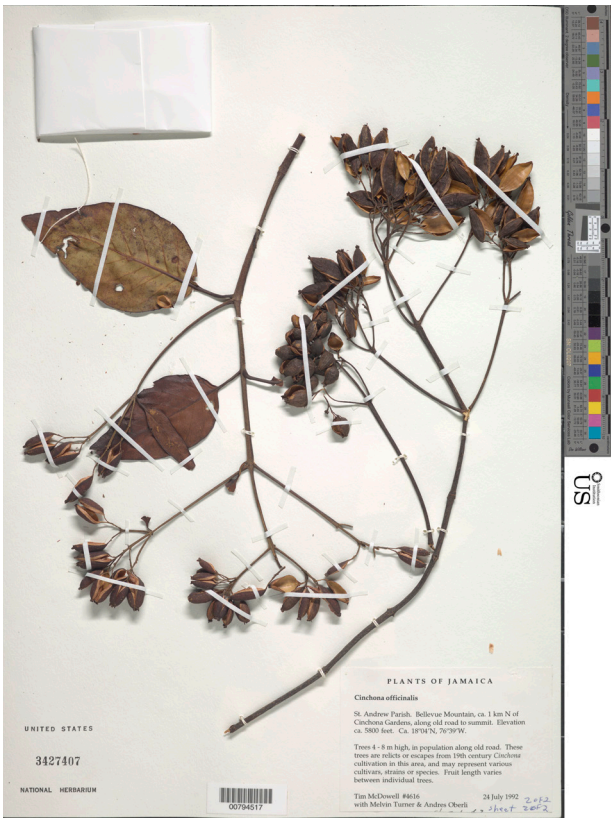


Figure 1. Herbarium specimen of *Cinchona officinalis*, one of the feverbark species used as a quinine source.

Fever bark trees (*Cinchona* spp.) are necessary for quinine, and native to the Andes mountains. Large-scale production of quinine occurred in the Dutch colony of Java. As early as 1940, Germany seized control of the Dutch quinine areas, and supplies were no longer available to the Allies. Then in 1942, Japanese troops invaded Java. I wonder why the US didn't see this coming. I might add, coincidentally, that the same situation occurred with rubber, which had military uses ranging from gas masks to barrage balloons. Rubber trees were grown commercially in Indonesia, so both of these products were under Axis control. Amsterdam was the center of pharmaceutical distributions for all of Europe, so once Germany controlled Amsterdam, the English were without much needed drugs. Before WWII, we had young men training in military camps in the South that were malarial swamps; the Office of Malarial Control [which eventually became the CDC] organized missions to Central and South America to bring back trees and seeds, but to grow trees from seed to harvest bark takes over a decade. This was not a viable solution in wartime. Fortunately, by 1944 quinine had been synthesized.

A lot of these medicinal plants seem perfectly designed for wartime scenarios, having a long shelf life, being easily preserved and transportable. Are there examples of (and could you elaborate on) medicinal plants that are useful for wartime scenarios but not really daily life scenarios in the US?

Of all botanical compounds, the single most important wartime drug was morphine [from opium poppies] for pain control in combat wounds. During the Civil War, the "soldier's disease" was opium addiction. During WWII, there were morphine doses that Squibb made in little pre-measured syrettes [single dose, hypodermic needle, injection unit] of morphine; field hospitals pinned empty syrettes to the uniforms of wounded soldiers to avoid overdoses. We cultivated fields of opium poppies as a source of morphine and related alkaloids. There was fear that thieves might steal poppy capsules for their opium-containing latex. A lesser known wartime use of opium was Paregoric, a tincture of opium (low doses of opium dissolved in alcohol) flavored with anise and camphor; in the 1950s, you could buy this over the counter for teething children. One of the side effects of opiates was constipation; it slows the muscles used for bowel movements; thus, Paregoric was also used to treat severe cases of dysentery, particularly during in the war in the Pacific.

The Germans used SEE (an acronym for scopolamine, ephedrine, and eukodol), developed as a multipurpose combat pharmaceutical administered in the field to injured soldiers. SEE caused the soldier to forget the horrific memories and be willing to go back out when healed (the effect of scopolamine from nightshades and belladonna); it also stabilized blood pressure (ephedrine) and reduced pain (eukodol derived from opium alkaloids, a.k.a. oxycodone).

Could you talk more about scopolamine and twilight sleep (Dämmerschlaf)?

Twilight sleep was developed in Germany by two doctors to provide a painless childbirth. The time of this development coincided with a downturn of the German population (after WWI), so when Hitler came to power, he was concerned with increasing births to supply the German military. Third Reich policy was to reward women who had a large number of children. Twilight sleep was used widely between the wars and even became popular in the US. It was advertised in magazines with endorsements from well-known women (Figure 2). The method was similar to SEE but omitted ephedrine. Scopolamine helped women to forget the pain, and opiates dulled the pain. Apparently, the dose was enough to cause incredible hallucinations, and some women required restraint. When twilight sleep was first advertised, it was the wealthiest

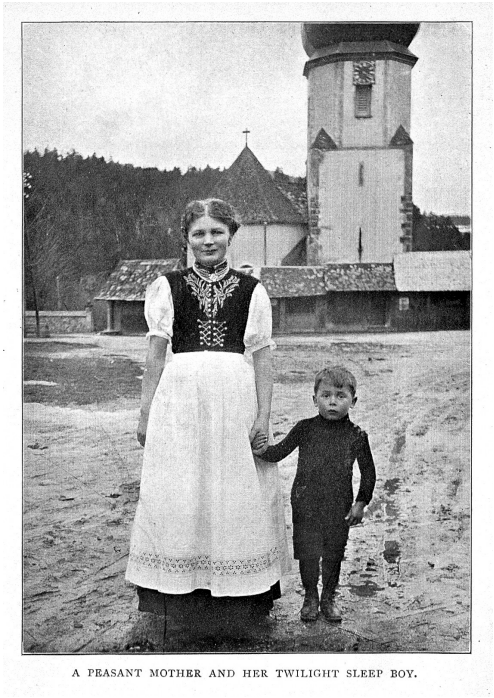

A PEASANT MOTHER AND HER TWILIGHT SLEEP BOY.

Figure 2. German mother and child illustrated in *Painless Childbirth in Twilight Sleep*, a text that promoted the use of this drug mixture during labor.

women who first used it, but the last hospitals to use this method during the 1960s were hospitals serving poor women. The irony is that German soldiers were likely born to women administered twilight sleep during birth; those who were wounded were given the same drugs on the battlefield. Dose is essential to the effect. Scopolamine can control motion sickness, settle the nerves, or even work as a truth serum at low doses; at higher doses it becomes an extreme hallucinogenic.

You briefly mention coconut water transfusions in chapter 7. This sounds so interesting! How was this discovered? Is this process still used today under any scenarios?

Immature coconuts contain liquid, which is actually the endosperm that provides nutrition for the young plant inside the coconut seed. I had come across a couple of references in first-hand accounts of combat, in which men were hooked up to coconuts in field hospitals and these were eventually confirmed by medical accounts. I think under desperate conditions, desperate things are done. Coconut endosperm is sterile, and it does contain some sugars and amino acids; it is slightly more dilute than human blood plasma, but the compounds were similar enough to keep some men from going into shock. There was research into other possible compounds to serve as plasma substitutes, including weak solutions of the fruit

pectin used in making jams and jellies.

Many of these originally naturally derived drugs are now produced synthetically. What are some of the advantages and disadvantages of this?

There are certainly more advantages to producing compounds synthetically or using GMO technology. Some plants are not easy to grow, and some crops will fail. We don't always know the growth conditions necessary for plants to synthesize the compound of interest, and levels of phytochemicals may vary depending on climate and other growth conditions. Of course, losing the knowledge of how to grow medicinal plants is unwise. Indigenous populations still rely on the whole plants and can use them effectively. However, on a large scale, the future for plant-based drugs is synthesis or partial synthesis or genetic modification and development. It's especially true when drugs are in bark, for instance the paclitaxel derived from Pacific yew trees. It proved effective in fighting breast and ovarian cancer, but bark removal resulted in the loss of trees.

Why did penicillin catch on more readily than other naturally derived antibiotic treatments that you mention, such as sphagnum moss and tea tree oil?

Penicillin was so incredibly reliable that we never saw anything like it. Sphagnum moss is probably more bacteriostatic, slowing the bacterial growth because it's so acidic. It was probably originally used because it's absorbent, but it also releases hydrogen ions, which lowers pH to acidic levels. Tea tree oil was also known since ancient times, but it wasn't as broad based as penicillin which can kill the bacteria that cause gas gangrene overnight. Penicillin also killed syphilis and gonorrhea, which was also important in and around army bases in wartime. The use of penicillin for STDs was not as widely publicized as its use for treating wound infections. It's hard to believe that we entered WWII without penicillin.

The County Herb Committee initiatives revealed that during wartime, women and children learned how to identify, collect, and dry useful herbs. Many modern Americans, including me, cannot do this. Is there use for understanding botany and medicinal botany in a world where we can easily stop by the drugstore for prescriptions?

Yes, there is. The County Herb Committees were organized in England when they found themselves without pharmaceuticals. When Amsterdam was under German occupation, the few drugs that the British could smuggle out were used for the troops. The Royal Botanic Gardens, Kew created manuals and directions for drying plants and encouraged people to harvest plants from fields and hedgerows. Collectors also dried algae for medicinal iodine and agar. There was nationwide collection of medicinal plants. The manuals didn't have illustrations of the plants, so it was assumed that people knew what they were and could go out and collect reliably and safely. There has been a recent concern that we don't have enough people in this country that know field botany, for whatever reason this might be needed. There has been a 50% decline in botany degrees since the 1980s and about half of the schools that once offered these degrees no longer offer the programs. Right now, the alternative is if you want to learn about botany and collect plants go to botanical gardens and arboreta, many of which have partnered with universities, where you can study hands-on botany. It's a practical field of science that has just been lost, but the knowledge is still there in books and could be revived.

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