Science AMA Series: I'm Cassandra Quave, a medical ethnobotanist. I study the botanical ingredients used in traditional medicines for infectious disease to discover new solutions for antibiotic resistance. AMA!

Cassandra$_{Q}uave^{1}andr/ScienceAMAs^{1}$

[1]Affiliation not available

April 17, 2023

Abstract

Hi, Reddit! Thanks to you all for these insightful questions! I've enjoyed the opportunity to discuss our research with so many interested people. I want to thank my lab team (especially Akram Salam, Dr. James Lyles and Dr. Angelle Bullard-Roberts) and the amazing Carol Clark at Emory Communications for their help during this event! Also - thanks to one of my favorite natural products (caffeine) for helping us power through the Reddit AMA marathon! I'm sorry if we did not have time to answer your question but hopefully you can find further information in some of the links posted during the AMA. In addition, please follow the Quave Research Group on Twitter https://twitter.com/QuaveEthnobot, Facebook https://www.facebook.com/QuaveMedicineWoman, Instagram http://instagram.com/quaveethnobot/, and our research group webpage http://etnobotanica.us/. I'm Cassandra Quave, a medical ethnobotanist at Emory University's Center for Human Health and Department of Dermatology in the School of Medicine. Ethnobotany is the study of human interactions with plants — especially in traditional societies that incorporate wild plants into their daily lives. My lab is focused on studying the botanical ingredients used in traditional medicines for infectious disease to discover new solutions for one of the world's most pressing medical issues: Antibiotic resistance. Traditional healers in the Amazon, for example, have used the Brazilian peppertree for hundreds of years to treat infections of the skin and soft tissues. We recently discovered that the red berries of this plant — an invasive, noxious weed common in Florida —contain a medicinal mechanism with the power to disarm dangerous antibiotic-resistant staph bacteria known as MRSA. This mechanism works by simply disrupting the ability of MRSA to produce toxins, so the body's natural immune system can work to better clear the infection. You can read more about this discovery here: http://esciencecommons.blogspot.com/2017/02/brazilian-peppertree-packs-power-to.html And here is a link to my web site: http://etnobotanica.us/ I'll be back at 1pm EST to answer your questions. Ask me anything!

the WINNOWER

REDDIT

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CASSANDRA_QUAVE R/SCIENCE

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I'm sorry if we did not have time to answer your question but hopefully you can find further information in some of the links posted during the AMA. In addition, please follow the Quave Research Group on Twitter https://twitter.com/QuaveEthnobot, Facebook https://www.facebook.com/QuaveMedicineWoman, Instagram http://instagram.com/quaveethnobot/, and our research group webpage http://etnobotanica.us/.

I'm Cassandra Quave, a medical ethnobotanist at Emory University's Center for Human Health and Department of Dermatology in the School of Medicine. Ethnobotany is the study of human interactions with plants — especially in traditional societies that incorporate wild plants into their daily lives. My lab is focused on studying the botanical ingredients used in traditional medicines for infectious disease to discover new solutions for one of the world's most pressing medical issues: Antibiotic resistance. Traditional healers in the Amazon, for example, have used the Brazilian peppertree for hundreds of years to treat infections of the skin and soft tissues. We recently discovered that the red berries of this plant — an invasive, noxious weed common in Florida —contain a medicinal mechanism with the power to disarm dangerous antibiotic-resistant staph bacteria known as MRSA. This mechanism works by simply disrupting the ability of MRSA to produce toxins, so the body's natural immune system can work to better clear the infection.

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Greetings from Australia. My question is simple but I'd like to hear what you have to say; what measures do you think global governments should take in addressing the issue of antimicrobial resistance before it reaches the point of no-return, excluding asking people to stop misusing antibiotics?

Edit: antimicrobial*

SplimeStudios

Thanks for this question. Yes, antimicrobial resistance is a major global concern. It is not simply an infectious disease problem, it is a MEDICINE problem. The loss of effective antibiotics will impact healthcare across the board - from surgical procedures, cancer therapy, and so on. Here are two useful reports and sets of guidance on how to address this challenge: the O'Neill report on Tackling Drug-Resistant Infections Globally (https://amr-review.org/) and the Pew Antibiotic Resistance Project (http://www.pewtrusts.org/en/projects/antibiotic-resistance-project). Some points that are commonly agreed upon across the scientific community are that we need to 1) eliminate the use of antibiotics as growth promoters in animal feed (antibiotics given in low doses to animals fosters development of resistance; 2) improve/develop point-of-care diagnostics (to have rapid ID of the responsible pathogen); and 3) expand our toolkit of new drugs (with a focus on increasing chemical scaffold diversity and exploring new mechanisms).

What, in your view, are currently the most promising antibiotic replacements? Do any of them have a shot at being as good or better than traditional antibiotics?

6hMinutes

It's not about replacing traditional antibiotics. It's about finding alternative ways to treat infections that don't raise antibiotic resistance. We need to expand our medicinal toolkit. In some cases, you need to go in heavily with antibiotics to treat a patient. But instead of always setting a bomb off to kill an infection, there are situations where using an anti-virulence method may be just as effective, while also helping to restore balance to the health of a patient. More research is needed to better understand how we can best leverage anti-virulence therapeutics to improve patient outcomes.

The latest classes of antibiotics introduced to the market were actually discovered between the 1950s and 1980s. Scientists have just been building off the same building blocks of earlier classes and modifying them slightly to create new antibiotics. Examining the extracts of plants used by traditional healers for infections may open up discovery of new chemical scaffolds for drug design, and provide important pathways for battling antibiotic-resistance.

I'm so excited for this AMA! This is such an interesting topic. Thank you!

Do you know of any good sources for more information on this topic; any books or websites you'd recommend? What's your opinion of the information offered in herbal healing books, in general?

EmrysMerlin

Here are some good sources:

Books Medical Botany (https://www.amazon.com/Medical-Botany-Plants-Affecting-Health/dp/0471628824/ref=sr_1_1?ie=UTF8&qid=1494004860&sr=8-1&keywords=Medical+Botany)

Dewick's Medicinal Natural Products (https://www.amazon.com/Medicinal-Natural-Products-Biosynthetic-Approach/dp/0470741678/ref=sr_1_1?s=books&ie=UTF8&qid=1494004479&sr=1-1&keywords=medicinal+natural+products)

Biology of Plants (https://www.amazon.com/Raven-Biology-Plants-Ray-Evert/dp/1429219610/ref=sr_1_3?ie=UTF8&qid=1494004531&sr=8-3&keywords=biology+of+plants)

Fundamentals of Pharmacognosy and Phyotherapy (https://www.amazon.com/Fundamentals-Pharmacognosy-Phytotherapy-Michael-Heinrich/dp/070203388X/ref=sr_1_1?ie=UTF8&qid=1494004776&sr=8-1&keywords=fundamentals+of+pharmacognosy+and+phytotherapy)

Eating on the Wild Side (https://www.amazon.com/Eating-Wild-Side-Pharmacologic-Implications/dp/0816520674/ref=sr_1_1?s=books&ie=UTF8&qid=1494006419&sr=1-1&keywords=eating+on+the+wild+side+nina+etkin)

The Origins of Human Diet and Medicine (https://www.amazon.com/Origins-Human-Diet-Medicine-Chemical/dp/0816516871/ref=pd_sbs_14_1?_encoding=UTF8&pd_rd_i=0816516871&pd_rd_r=ATDC8YB48N1H2TS7X84C&pd_rd_w=zYebJ&pd_rd_wg=zAAqF&psc=1&refRID=ATDC

Florida Ethnobotany (https://www.amazon.com/Florida-Ethnobotany-Daniel-F-Austin/dp/0849323320/ref=sr_1_1?ie=UTF8&qid=1494006266&sr=8-1&keywords=florida+ethnobotany)

Native American Ethnobotany (https://www.amazon.com/Native-American-Ethnobotany-Daniel-Moerman/dp/0881924539/ref=sr_1_1?ie=UTF8&qid=1494006230&sr=8-1&keywords=native+american+ethnobotany)

African Ethnobotany in the Americas (https://www.amazon.com/African-Ethnobotany-Americas-Robert-Voeks/dp/1461408350/ref=sr_1_1?ie=UTF8&qid=1494006185&sr=8-1&keywords=african+ethnobotany)

Traveling Cultures and Plants: The Ethnobiology and Ethnopharmacy of Human Migrations (https://www.amazon.com/Traveling-Cultures-Plants-Ethnopharmacy-Environmental-ebook/dp/B00EDY6AVM/ref=sr_1_1?ie=UTF8&qid=1494006139&sr=8-1&keywords=traveling+cultures+and+plants)

Plants, People and Culture: The Science of Ethnobotany (https://www.amazon.com/Plants-Culture-Paperback-Michael-2005-12-23/dp/B01NH01YZP/ref=sr_1_1?ie=UTF8&qid=1494005994&sr=8-1&keywords=balick+and+cox)

Websites Quave Research Group (http://etnobotanica.us/) Emory Herbarium (https://scholarblogs.emory.edu/emoryherbarium/) National Center for Complementary and Integrated Health (https://nccih.nih.gov/) National Center for Natural Products Research (https://pharmacy.olemiss.edu/ncnpr/) Center for Natural Product Technologies at UIC

(http://cenapt.pharm.uic.edu/) Journal of Natural Products (http://pubs.acs.org/journal/jnprdf) American Society of Pharmacognosy (http://www.pharmacognosy.us/) Society for Economic Botany (http://www.econbot.org/) Economic Botany (http://www.springer.com/life+sciences/plant+sciences/journal/12231) US National Librar(y of Medicine's PubMed (https://www.ncbi.nlm.nih.gov/pubmed) Tropicos (http://www.tropicos.org/) International Plant Names Index (http://www.ipni.org) WHO Guidelines on Good Agricultural and Collection Practices for Medicinal Plants (http://apps.who.int/medicinedocs/en/d/Js4928e/) Convention on Biological Diversity (https://www.cbd.int/) Antibiotic Resistance Threats in the USA (https://www.cdc.gov/drugresistance/threat-report-2013/)

Opinion of herbal healing books: Herbal healing books run the full gamut from remedies based on anecdotal evidence to remedies that have been subjected to some level of scientific testing. As with anything else, you would be well advised to check the credibility of the sources used.

Suppose a traditional community uses Plant A for generations to heal X. You discover the mechanism behind it, it becomes a patent, you get scholarly recognition and the industry gets richer.

My question is, does the traditional community who originally discovered this plant's utility get anything out of it in the end?

lastpawn

Thanks for this question. Yes, current international conventions address this issue. Mechanisms for access and benefits sharing are in place to ensure that communities receive benefits from the research. The international agreement on Access and Benefit Sharing was established by the Nagoya Protocol in 2010 (https://absch.cbd.int/).

Sadly, throughout history, there are of course examples of biopiracy in which the traditional knowledge was exploited without any credit or benefit to the original knowledge holders. However, most countries and universities are now aware of the issues and work to prevent future problems using these guidelines.

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Can you share with us, one particular plant that is so amazing & multipurpose that people should have it in their garden

HolyShitzurei

This is such a difficult question for me! It's hard to narrow my choice down to one plant - but I will tell you what I currently have growing in my own home medicinal plant and culinary herb garden: clary sage, basil, holy basil, oregano, borage, chamomile, calendula, marsh mallow, aztec sweet leaf, evening primrose, peppermint, spearmint, catnip, lemon balm, and rosemary! I love combining holy basil (Ocimum sanctum) with mixes of catnip (Nepeta cataria) and lemon balm (Melissa officinalis) as a tea.

Hi Cassandra, I'm a First Nations person from Canada who was raised with small bits of traditional medicine knowledge. I'm very happy to hear you are working with traditional knowledge holders to combat the very serious problem of antibiotic resistance in the modern world. Do you find it difficult to

establish trustful relationships with Indigenous Medicine People?

qualiawiddershins

Hi, thanks for your question. It touches on a key factor in ethnobotany, that of building trust and working in a collaborative and ethical way with local communities. We work closely with community leaders to explain the goals of our work and get their consent along with the prior informed consent of every individual that is interviewed in our field studies. This is key to building trust and a truly collaborative relationship with community members. As a medical ethnobotanist, I closely follow the ethical guidelines set forth by the International Society for Ethnobiology. The full code of ethics is available here (http://www.ethnobiology.net/what-we-do/core-programs/ise-ethics-program/code-of-ethics/code-in-english/).

In addition to ISE, members from other societies like the Society for Economic Botany also follow this code. In addition, we also follow the guidance set forth by the Convention on Biological Diversity (https://www.cbd.int/) and the Nagoya Protocol on Access and Benefit Sharing (https://www.cbd.int/abs/). Some of the ways that we've engaged in early access and benefit sharing with communities is by returning the local knowledge recorded to the communities in booklets written in their language; building ethnobotanical gardens; training students from other countries in laboratory methods in my labm and so on.

Is it true that pharmaceutical companies synthesize these natural compounds because you cannot patent "a berry"? Is there a big difference between the medicine in natural vs synthesized form, in equal amount/concentration?

hashtagfrugal

Thanks for the question. If there happens to be a chemical found in a species of berry that has very desireable medicinal properties on its own, then synthesis could be a potential route to explore for scaling up production of the compound. This does not necessarily increase the patentability of the compound though. It would need to be modified structurally such that the structure is novel and different from what is found in nature. In other words, there are specific issues to address when working with natural products. Patent laws differ by country and a product can be patented in multiple countries. Focusing on the United States here, patenting natural products has recently been put into the spotlight. In 2013, the Supreme Court case Association for Molecular Pathology vs. Myriad Genetics Inc. ruled against patenting of naturally occurring entities such as genes. Due to this case and others before it, the court issued a memorandum on patent eligibility for natural products. This document states that a patentable product must be significantly different from its naturally occurring form. Therefore, a biologically active natural product must be modified if it is to be patentable. This lends to the following possibilities for patentable entities. One could possibly patent the altered product itself, the method of production, or a novel use of the product. If the constituents of the product cannot be fully determined, a product-by-process patent may be considered, if there are no other means of patentability. This does not include products synthesized from a new process that are identical to a naturally occurring product. For one to patent the method of production, the method cannot simply be common knowledge or general application of the product. The specific dosage, regime, and disease target must be stated.

Regarding your question on the difference between a natural and synthetic compound: Every chemical that exists has a unique chemical structure. What synthetic chemists do is basically build these structures in a lab. In a sense, a plant has its own lab inside its cells full of chemicals and enzymes that modify them in order to come up with the final suite of compounds. Take a natural product like kaempferol, for instance. The kaempferol that a plant makes and the kaempferol that a chemist makes are exactly the same. If they were different, then what the chemist made was not, in fact, kaempferol. Note that, in general, natural products are much larger and more complex than totally synthetic compounds, which is what is usually produced by chemists. Therefore, for a chemist to synthesize a natural product from scratch can range from being somewhat challenging to nearly impossible. In the latter cases, simpler natural products that are commercially available are used as a starting point, and the chemist modifies those in order to form the final natural product. Taxol is a natural product and a crucial cancer medicine with which this approach is taken.

Have you studied oregano oil and if so, what bacteria is resistant to it?

what-am-i-doing1

We have not studied oregano oil, although it has been shown to have antibiotic activity against certain strains of bacteria in the laboratory. Please refer to the 2016 scientific review of oregano oil by Rodriguez-Garcia, et al: Oregano Essential Oil as an Antimicrobial and Antioxidant Additive in Food

Products (https://www.ncbi.nlm.nih.gov/pubmed/25763467). Note that such laboratory findings for essential oils are not uncommon, but they do not mean that the EOs will have the same success at treating a condition as a developed medicine.

How do you decide which plants to study from the long list of wild and (at least supposedly) medicinal plants?

EmrysMerlin

Excellent question. First of all, I have specialized in the plants of the Mediterranean, so I primarily focus my studies on that geographic region. I review the ethnobotanical literature of that region and also conduct ethnobotanical field studies with collaborators. We work closely with local communities in a collaborative way and conduct interviews with people interested in engaging with our work. These interviews are conducted with hundreds of people at a time in order to learn which traditional remedies are known and what recipes are agreed upon in general. I focus specifically on skin infections, so I focus on relevant remedies and on collecting the corresponding plants.

Additionally, it is convenient to work with my Emory University students locally, and we also collect plants that are near Atlanta. I do large-scale plant collecting in the states of Georgia and Florida. These collections are guided by the existing ethnobotanical and herbal medicine literature concerning past and present uses of the flora of this region. These plants are typically extracted back in my lab and screened for medicinal activity against an array of infectious pathogens.

What are some threatened or endangered species that would help prevent or cure infections but are too rare to cultivate for medicine?

Spiwolf7

Thanks for the question. Here is an example that you may find informative: Taxol is a cancer drug derived from Taxus brevifolia (Pacific yew tree). When the discovery was made, T. brevifolia was already becoming scarce, and so it was never commercially harvested from its habitat. Scientists developed a method to produce taxol at a large scale only when a chemical similar to taxol was found in extracts of other species of yew trees. Scientists isolated these chemicals and were able to make relatively simple modifications to them in order to synthesize the final taxol product. This approach would be a possible course of action in cases such as the one you have described.

Hi Cassandra, thanks for the AMA. Is antibiotic-resistance at a problematic level inevitable at this point in your opinion? Are there many examples so far of traditional medicines being effective as in your example? How far do you think this will go towards compensating for antibiotic resistance?

buzzbuzz_

Interesting question! Antibiotic resistance is already problematic. The CDC estimates that each year in the U.S., 2 million individuals acquire antibiotic-resistant infections and 23,000 individuals die as a direct result of those infections. And the potential of this problem to become a global health crisis is very real. At present, our arsenal of antibiotic treatments is comprised of single compounds that, when they get into bacterial cells (a bacterium is one cell), they disrupt biological processes of the cell that are crucial for survival, such as the maintenance of the resilience of the cell wall. The fact that the chemicals kill the bacteria forces a population of bacteria to try to develop resistance against it, and this occurs genetically. The fact that the treatments are single chemicals means that the bacteria can easily develop resistance because it has only one entity threatening it. Plants used in traditional medicine for their antibiotic activity contain not just chemicals that kill bacteria, but also chemicals that shut down bacteria's virulence, inhibit the production of biofilms, etc. Additionally, they contain numerous medicinally active chemicals. Translating these two characteristics into novel antibiotic drug development is one way to combat antibiotic resistance.

I just read about you for my botany class at Penn State University!

What is the most interesting plant you've come across? Why do you find it so interesting?

KinkyKittenHeather

Hmmm... this is a tough one. There are so many interesting plants that I've worked with over the years. I'm most interested in understanding human uses of wild plants. One really neat one that has multiple uses is Arundo donax - or the giant reed - in Poaceae (grass) family. In southern Italy, this plant is

used as a tool (as a fork and wine barrel tap), in construction (to build grain bins, fencing for gardens, vineyard support), as a bartering stick (items that are traded are tracked by carved notches on the reed), as bedding (the leaves once were used to stuff mattresses), and as a medicine (the white internode membranes are used to stuff bleeding lacerations as a hemostatic). So many amazing uses from what some would just see as a weedy grass!

The exiting bit for me seems to be the ability to prevent or reduce biofilm formation. Did you test if it could affect established biofilms?

What made you test this on staph? Did you get negative (less positive) results testing it on others (Pseudomonas, Candida etc)?

Thanks!

Orkran

Great question! Yes, the prevention of biofilm formation is indeed an exciting activity. We have not yet assessed the activity of this extract in biofilm eradication. It is in our lineup of future experiments to examine this with biofilm attached to different materials. Regarding other pathogens, this extract did have some very nice activity against two other important human pathogens and we are working on additional experiments and publications to report these activities. Interestingly, it did not inhibit growth of several commensal skin bacteria, which was good for avoiding dysbiosis of the skin microbiome. You can access the full paper here: https://www.nature.com/articles/srep42275

How did you get to your position, in terms of education and career choices? You have my dream job. I want to find a plant that will help manage or eliminate symptoms of mood disorders and fibromyalgia one day.

veritasviriditas

Thanks so much - it was a long path to get where I am today. You can get a sneak peak at my journey in these stories: http://www.emory.edu/EMORY_MAGAZINE/issues/2012/autumn/of_note/quave.html and https: //www.nytimes.com/2016/09/18/magazine/could-ancient-remedies-hold-the-answer-to-the-looming-antibiotics-crisis.html?_r=0

I'm also currently writing an autobiographical book about my life in science that touches on the challenges I've faced as a disabled woman and mother pursuing a high paced, demanding career in science.

Well, I'm but a humble dentist, is there anything new on the horizon to treat periapical apical infection? (Tooth infection)

We've been using the same antibiotics for a ridiculously long amount of time (Main line of treatment: Betalactamics [aka penicillin derivatives]).

And we're reaching an era where a lot of people don't want "more chemicals [aka pills]" so an alternative to what we currently have would be most useful. I know it's not here yet but , maybe it's on the horizon.... I'm not sure, you guys are way better informed about botanical breakthroughs which is why I ask.

TheMythof_Feminism

Dear dentist: thanks for your question! Bacterial biofilms present a major hurdle for dental care. In addition to our work on quorum sensing and growth inhibitors, we are also working on biofilm inhibitors from nature. There are many interesting medicinal plants used in indigenous dental care - such as teeth blackening practices and the use of chewing sticks. Some of these plants have demonstrated interesting anti-biofilm properties and may hold some potential in broader dental applications in the future.

What are some of the more interesting or exciting discoveries you've made?

EmrysMerlin

I think that some of our most exciting discoveries have been on the following plants: Rubus ulmifolius (blackberry roots) for blocking biofilm formation in MRSA; Castanea sativa (chestnut leaves) and Schinus terebinthifolius (Brazilian Peppertree) for blocking bacterial quorum sensing. Each of these

plants are used in traditional medicine for inflammatory or infectious skin disease - but worked via alternative pathways (non growth-inhibition) and finally provided an explanation for why and how these worked in these traditional medical applications. Here are some publications on these particular findings:

Muhs, A., T. Lyles, C.P. Parlet, K. Nelson, J.S. Kavanaugh, A. R. Horswill, C.L. Quave. (2017) Virulence inhibitors from Brazilian Peppertree block quorum sensing and abate dermonecrosis in skin infection models. Scientific Reports 7: 42275 doi:10.1038/srep42275

Quave, C.L., M.E. Carmona, C.M. Compadre, G. Hobby, H. Hendrickson, K. Beenken, and M.S. Smeltzer. (2012). Ellagic acid derivatives from Rubus ulmifolius inhibit Staphylococcus aureus biofilm formation and improve response to antibiotics. PLoS ONE 7(1): e28737.

Quave, C.L., J.T. Lyles, J.S. Kavanaugh, K. Nelson, C.P. Parlet, H.A. Crosby, K.P. Heilmann, A.R. Horswill. (2015) Castanea sativa (European Chestnut) leaf extracts rich in ursene and oleanene derivatives block Staphylococcus aureus virulence and pathogenesis without detectable resistance. PLoS ONE 10(8): e0136486. doi:10.1371/journal.pone.0136486

I am very happy to see an AMA in my field of study. I do have a couple of questions for you if you allow me:

1) We did some research on our side on the essential oils of Schinus molle and did discover the presence of chemotype in the volatile production (the differentiation was on the shyobunol terpene family). Have you had the chance to see some indication that the active compounds in the fraction may be linked to a peculiar chemotype?

2) One of the problems with natural extract and isolate is that in the current pharmaceutical regulation, you generally need to prove that a drug needs to either be more efficient than one already established or answer a different version of the problems. Do you think that natural drugs will eventually have the acknowledgement that they deserve even though they may not be as strong as established pharmaceutical compounds?

3) Have you tried to test individual compounds for their activity? If so, have you noticed synergistic effect. If so, are you planning on establishing this effect.

BlindAngel

There is always the possibility of the activity being associated with a specific chemotype of a plant. So many things can influence what secondary metabolites are produced by an individual plant- water stress, infections, amount of sunlight, soil conditions, herbivory. Our samples for this study were pooled from several different individuals across different collection sites in order to minimize the influence of any particular chemotype.

I think Natural products will always have a role in human health. A significant portion of the world population still uses Traditional Medicine and Natural Products; the WHO shows 30-90% of the population, depending on the country (http://apps.who.int/medicinedocs/en/d/Js2293e/).

We use bioactivity guided fractionation to identify the active compounds and are in the process of fractionating, isolating, and testing these. If activity is lost at a specific fractionation step then we will begin testing for synergistic activity using a checkerboard assay. In addition we often test isolated compounds for synergy with known pharmaceuticals using the same assay.

No question, just a thank you for helping to save your terrestrial brethren from grief and death. Scientists and researchers like you redeem our species.

BabeOfBlasphemy

Thanks :)

Is marijuana part of your study? If so what have you found? Curious to know where thc oils stand, particularly in fighting inflammation

homesickATLien

Hi - thanks for your question. No, we don't currently study Cannabis in our lab. This is for 2 reasons: 1) getting permits from the government to study this even in scientific laboratories is exceptionally onerous and difficult; and 2) Cannabis does not really have any anti-infective traditional uses and is thus not a major lead for us to explore for the discovery of new drugs to treat infections.

Despite being one of the largest plant families based on number of species and one of the most diverse based on geographic distribution and morphology, orchids are noticeably under represented in terms of food and medicinal applications, with Vanilla and Dendrobium extracts being about the only common examples I can think of. Have any orchid species come under your radar? I know that numerous orchid species have been used in traditional medicines, so it's not as if there is no precedence for investigating them.

LammergeierAteMyBone

We haven't worked with any orchid species yet. Orchids are protected under CITES (https://www.cites.org/) and are thus not included in our studies. You are correct though, they seem to be very underrepresented in terms of food and medicine. There are many orchids, especially in SE Asia, that are eaten locally- including as an ice cream. In the Balkans, terrestrial orchids are collected to make a special drink called salep. This would be an interesting area of research if it could be done with species in cultivation so as not to impact threatened wild populations.

Do you study the anthropology of it at all, or are you focused on studying the plants and drugs themselves?

I'm always curious about what leads to cultures (including our own, prior to our development of scientific investigation methods) to figure out what plants work for what effects and so on. Do they have investigative methods? Or is it centuries of sheer luck and happenstance? Something else?

Lord_Steel

Understanding the human context of plant use is one of the most critical aspects of what we do. As I mentioned in answering another question, a significant part of our work involves talking directly to the people who are using the plants to ascertain the context in which they are used. The plants that we look at in my lab are typically plants that have been used by different ethnic groups in the context of skin infections.

As for the origin of cultural plant use, there are various ways that an ethnic group may come to identify the usefulness of a plant. Although there were often mythological aspects to plant selection, there are many plant use patterns across different cultures that suggest independent discovery and or trial and error. Often, organoleptic properties of a plant may provide initial clues to its phytochemistry--many pungent smelling and aromatic compounds are great antimicrobials. If a plant is effective for one health concern, then it may be tried for other ailments and so on.

My question is: with your experience, could you estimate the percentage of common drugs that could be replaced with more plant-based medicine? if so, what would that percentage be?

JNMMP

Thanks for your question. First of all, many of our existing common drugs were originally discovered in plants. In some cases, these were slightly chemically modified to increase activity or reduce toxicity, and many are now produced via synthetic means - but their origin was in nature. In reference to replacements, please see my response to a previous question: https://www.reddit.com/r/science/comments/69e7ni/science_ama_series_im_cassandra_quave_a_medical/dh6fsqt/

What led you to working in ethnobotany? Do you work with the more anthropological side of it, or it your job much more chemistry and biology heavy?

astycakes

I've always loved spending time in nature - and ethnobotany gave me the perfect opportunity for merging my passions for medicine, culture, chemistry and nature! It has been a long and winding path that took me to this career. I'm actually writing a book about it - stay tuned in the next year! Regarding the anthropology - yes, I absolutely apply anthropological methods in this work. I balance my time between field research working with communities and collecting plants, along with directing a team of scientists that work in the Emory Herbarium (https://scholarblogs.emory.edu/emoryherbarium/), my phytochemistry lab at Emory, and my microbiology and cell culture lab at Emory for bioassay testing. I'm so fortunate to have a fantastic multidisciplinary team that contributes to all of these research endeavors.

Do you conduct clinical trials that show effects surpass that of the placebo?

FoolioDisplasius

Thus far, our work has been based on in vitro and animal studies. Our next step is to move to clinical trials (pending funding) to assess the safety and efficacy of our top compositions. We will most likely use the FDA's botanical drug pathway, which allows for the testing and approval of botanical drugs (made up of multiple compounds from the same plant) - but which is also subjected to the same rigorous testing as a typical single compound drug.
https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM458484.pdf

Do you often find that the plants you study actually have the medicinal value that is ascribed to them?

EmrysMerlin

Great question! I'm most interested in plants that are used to treat infectious and inflammatory disease. One point I like to bring up often in papers and in meetings is that we need to broaden the types of assays used to assess the potential medicinal activity of a plant. For example, as described in our paper on Brazilian peppertree, the extract had limited impact on S. aureus growth. However, it worked instead by blocking the ability of the bacteria to communicate with one another. In animals - it was able to attenuate the formation of an infectious lesion (large sore) in the skin. This would have never been discovered if we had limited ourselves only to assays addressing standard antibiotic (growth inhibitory or killing activity). I think that in many cases, we just haven't asked the right questions yet to uncover the secrets of their activity.

Lately there's been a lot of debate in the horse world about topical wound ointments, especially since new laws this year mean you need an Rx for any veterinary antibiotics (used to be able to buy everything otc). I'm seeing silver compounds and tea tree oil honey pop up a lot. Are there are any interesting topical treatments in your research?

Also, how important do you think the restriction and proper use of topical antibiotics is in the scheme of antibiotic resistance?

Thank you for your time! Your research is fascinating!

nefariousmango

Hi - yes, we are definitely working on topical applications for chronic infected wounds, which could also potentially be relevant to the veterinary community. These sorts of chronic wounds often contain multiple species of bacteria. We need to undertake more work with polymicrobial biofilm models to really get a better sense of how these natural products might act in such a (more realistic) infection context.

Can you describe your approach? For example, I imagine that you become aware of a traditional medicine technique, gather information about the technique (applications, applicators, patients) and the ingredients, study the composition of the ingredients and the efficacy of the technique, then try to discover the active chemicals in the ingredients, and finally consider how to bring this technique to situations outside of its original traditional use...this is a lot of work!

To what extent does genomics improve your ability to study ingredients and to develop new solutions? (Assuming it is used in understanding the ingredients and analyzing and comparing all studied ingredients)

sequel_injection

We use ethnobotany to guide our research program. This entails spending time outside of the lab, interviewing people where they live. The majority of my field sites are in the Mediterranean. I speak Italian and work with local guides and translators when working in the Balkans, where multiple languages are spoken. After informing the individuals of our research and gaining both individual and community consent, I ask them about what plants they use to treat infections, skin injuries, stomach issues, care for their livestock. Much of the interview is unstructured and listening is a key skill. Often I am able to have the informant take me to the plant and show me how they use it. After this, I would collect a botanical voucher and if there is enough material make a bulk collection. The voucher is deposited with a local herbarium and a duplicate is sent back to the Emory Herbarium (https://scholarblogs.emory.edu/emoryherbarium/).

The bulk sample is dried in the field and sent back to the lab for further processing. Once in the lab, the

plant is frozen to kill any plant pathogens and then re-dried and ground into a powder. Most of our samples undergo a double maceration with an alcohol and aqueous decoction. The organic and aqueous extracts are concentrated and dried to a powder. Although often it is sticky maple syrup consistency and not an easy to work with powder. The dried extracts are brought up in a suitable solvent for bioassay and screened using one of your microbial assays. Extracts that are effective in the assay are further tested to determine the IC50 and IC90 value, the concentration of extract that inhibits 50% and 90% of microbial growth or other activities (biofilm, quorum quenching, etc). If these values are interesting then the extract is flagged for further workup. We also counter-screen extracts against skin cells to ensure that they are nontoxic to human cells.

A crude extract undergoes liquid-liquid partitioning to yield 4-5 partitions which are again tested in a bioassay. Any active partitions are then further refined often using a chromatographic technique flash chromatography or high performance liquid chromatography (HPLC). The resulting fractions are again tested by bioassay. The active fractions undergo further chemical isolations, and the process repeats until a single compound or group of compounds are identified using tools like LC-MS and NMR.

What is your favorite flower?

cheezeburger69

I love the beautiful flowers of the Protea genus. I had the opportunity to travel in South Africa two years ago and was just blown away by their beauty in the wild.

As you are probably aware, there is a lot of pseudoscience surrounding traditional remedies. How can lay people distinguish the real science surrounding these remedies from the exaggerated claims of "alternative medicine"?

Empigee

There are a lot of cases where the individuals behind the pseudoscience are able to present their claims in a manner such that a non-scientist would believe. This is because people behind some pseudoscience have knowledge of biology and/or chemistry, but their motivation may be profit driven. This is a very difficult question to answer. I would definitely encourage a non-scientist to seek advice from publically available resources such as the National Institutes of Health, National Center for Complementary and Integrative Health (NIH/NCCIH) website for useful information: https://nccih.nih.gov/ In addition to this resource, note that scientific findings are almost always published in scientific journals. PubMed (https://www.ncbi.nlm.nih.gov/pubmed) is one of the best databases to search through the biomedical literature. Before scientific findings are published, they are reviewed by other expert scientists to ensure robust research practices were used. There is a limit to how much a lay person could utilize this, though. Even peer-reviewed scientific findings must be critically analyzed to ensure that the conclusions drawn from the presented data are reasonable, and that is a job for a scientist.

The title of your ama (including your name, you have an amazing name) sounds like the synopsis of a great tv show. Exploration! Science! Healing the sick! Saving the world! Go Cassie go!

mammalian

Thanks so much! I'm actually working with a production company to get a TV show off the ground to show the world all of these amazing plants! Fingers crossed :) In the meantime - have you seen Origins on Nat Geo - I made a cameo in the first quarter of the "Cheating Death" episode: http://channel.nationalgeographic.com/origins-the-journey-of-humankind/episodes/cheating-death/

What do you think of traditional Chinese medicine? Are there any herbs or plants that we should pay more attention to?

kenjitheshibainu

I have great respect for Traditional Chinese Medicine. It is an extremely deep field requiring intensive study, and there are scientists and TCM practitioners that have dedicated their careers to studying this fascinating system of medicine. I have focused my work primarily on traditional medical practices of the Mediterranean, but can provide some explanation of the TCM system of healing. A TCM doctor could treat two patients, each with the same disease, but would prescribe different herbal remedies to each based not only on the manifestation of the disease but also on the patient's innate physiology. TCM is a great example of personalized medicine. The medical formulas used are often combinations

of several plants, and thus are incredibly chemically complex. In contrast, my laboratory is currently studying plant extracts, one plant at a time, for the identification of medicinally active compounds and combinations thereof.

What is your response to people who "don't believe" in natural medicine?

tarrawr

There is so much that we have to learn from nature! If you look back to the origins of many of our leading drugs (aspirin, morphine, digitoxin, taxol, vincristine, artemisinin, and so on) - these were all originally isolated from plants and most had some use in traditional medicine by humankind in the past. Nature is an amazing resource for drug discovery!

Hey Cassandra, greeting from India, i have questions

1. Why cant human body develop like bacteria and viruses? We can see in just last 10 years most of the disease pathogens evolved with higher immunity but human are in same old place.
2. How do you think we will fight till when with diseases shielding with other microbs??

Edit: typos and language abnormalities

Prabir007

I didn't understand the second part of your question. The first part is very interesting! The difference basically lies in the ability of bacteria and viruses to replicate rapidly. Bacteria are single-cell organisms. A bacterial cell can divide very rapidly depending on the species. That is actually one way through which a bacterial cell can acquire new genes that could endow new biological functions to the cell. Cell division involves replication of DNA. When DNA is replicated there is a chance certain genes won't be replicated 100% exactly as the originals -- when this happens that gene has been mutated, so effectively a new gene has arisen. The mutation may make no effective difference in the biology of the cell, or it may make a huge difference, or it may set the stage for another mutation to make a huge difference -- there are all sorts of possibilities. Another way bacteria can acquire new genes that introduce new biology into the cell is via conjugation (gene transfer) with a neighboring bacterium. That can even occur between bacteria of different species! Once these new genes are acquired, they could potentially spread rapidly because bacteria divide rapidly. Examples of new biological functions endowed by mutations or new genes include: pumps in the cell wall that pump out antibiotics, enzymes that bind antibiotics and break them down, etc. It is through such acquired genetic changes that bacteria can develop resistance to antibiotics.

Viruses replicate rapidly as well, though via a much different mechanism, and as such can develop resistance to anti-virals.

There are a lot of articles out there that suggest that antibiotic resistance could lead to the end of modern society.

Do you think that the threat is that serious? Are you confident that there enough traditional medicines with promise that we will be safe from this doomsday scenario?

redlpine

I'm a fan of history. We know that human populations have expanded and contracted over time with the introduction of new disease agents. We are facing a serious threat to modern medicine, however, I wouldn't go so far as to say that it will lead to the end of modern society. The rise of antimicrobial resistance will have large human and economic costs and much more investment in science that approaches this issue from multiple angles is greatly needed. Here are some useful links on the AMR threat: http://www.who.int/mediacentre/factsheets/antibiotic-resistance/en/ and https://www.cdc.gov/drugresistance/

Lastly, I'll leave you with a bit of humor to lighten up this post :)

2000 BCE: Here, eat this root.

1000 AD: That root is heathen. Here, say this prayer.

1850 AD: That prayer is superstition. Here, drink this potion.

1940 AD: That potion is snake oil. Here, swallow this pill.

1985 AD: That pill is ineffective. Here, take this antibiotic.

2016 AD: That antibiotic is ineffective. Here, eat this root.

-Unknown source

I see that you mentioned that your work with plants, but what about fungi? I think there is a lot of potential to collect antibiotic derived from fungi as they custom make enzyme to fight off infections or foreign substances they get in contact with.

McStalina

We do collect and research several macrofungi in our group. Many of the current lines of antibiotics were identified from soil fungi. There are discovery efforts focused on "unculturable" fungi, bacteria, endophytes, and other fungal sources as well underway in other research groups.

I've recently discovered a love for bartending, and one thing that really fascinates is how varied and deep is the role played by plants. Many spirits, such as gin, were historically marketed as having medicinal properties. Can you comment on this? Is it possible to gain any medicinal or nutritional benefits from the botanical ingredients in spirits, liqueurs, cocktails, etc? Can you think of any drinks which currently provide those benefits, or suggest ways of producing such drinks? I'm not very familiar with botany, so do you have any thoughts on the medicinal properties of plants consumed as beverages about which I might not think to ask?

DanishPastry

Hi! Great question - and yes, you are absolutely right. There is a long history of botanical ingredients prepared in tinctures or used to flavor alcohol that also have medicinal attributes. One great example is the classic gin and tonic. Tonic water actually contains a bit of quinine - from Cinchona bark - which gives it that lovely bitter taste. In the past, British soldiers were given gin and tonic as a prophylactic against malaria. Here's another neat bar trick: if you hold (real) tonic water up to a black light, it will fluoresce in green! For a modern ethnobotanical twist on bitters - check out Roots and Shoots Bitters, which was founded by 3 female ethnobotanists http://www.shootsandrootsbitters.com/

What do you think of homeopathy?

123Surf

Great question. The short answer is that homeopathy, which is based on heavily diluted formulations, has absolutely zero basis in pharmacology and goes against all laws of physics. Homeopathy is NOT the same as naturopathy or herbal medicine - which DO include pharmacologically active levels of compounds from plants.

I'd like to take this as an opportunity to provide some background on homeopathy to the readers. This is an excerpt from my textbook (in progress) on Medical Botany:

Homeopathy was introduced as a form of medicine in the 18th Century by the German physician Samuel Hahnemann (1755-1843), though it may have longer historical roots. It is based on the concept of "like cures like", in opposition to allopathy "opposite cures opposite", or treating disease by agents that elicit effects different than those of the disease treated. Homeopathy uses materia medica of plant, animal and mineral origin in the preparation of medicaments. Examples include onion, chamomile, arnica, white arsenic, crushed whole bees, belladonna, and stinging nettle. However, the preparation of homeopathic remedies differs greatly from those of medical herbalism traditions as the material is heavily diluted with excipients, such as water, alcohol, or sugar. Materials may be diluted to one part of the material in 10,000 to even a billion or trillion parts of the solution. Under this system, the perceived effectiveness of the final formulation is greater when more dilute and is based on the concept of "water memory", or molecular memory of the material in the solution in which it is diluted. As the proposed mechanism for homeopathy does not follow the widely accepted laws of physics, chemistry, or pharmacology, it is subject to much criticism.

There are a few different systems used to denote how dilute the homeopathic remedy is. Historically, the centesimal or C scale was used, and refers to dilutions by a factor of 100 at each stage. For example, a 2C dilution would entail diluting 1 part of the substance in 100 parts of excipient, and then 1 part of this solution to be further diluted at 1:100, yielding a final dilution of one part material in 10,000 parts excipient. Likewise, a 5C dilution would yield one part in ten billion, a 6C dilution would yield one part in one trillion, and so on. Today, other forms of notation are more common for describing the final dilution level of a homeopathic remedy. For example, one might find bottles labeled with a "D" followed

by a number or an "X" preceded by a number. This refers to dilutions by decimal potency, and uses a factor of 10 at each dilution stage. For example, a homeopathic remedy labeled as D6 in dilution factor would be equal to one part material in 10^{-6} of excipient, or one part in a million. This would be of the same dilution factor as a remedy labeled as 6X. Most commercially available homeopathic products available on the market today range in dilution factors of 3X to 6X, or one part in one thousand to one part in one million. Products with very low dilution factors may exhibit some pharmacological effect depending on the dose administered, and may also present potential for side effects or drug interactions. Overall, however, an overwhelming number of scientific studies and clinical trials on homeopathy have revealed that its effects are no different than placebo. Despite the lack of scientific evidence, according to the 2012 National Health Interview Survey, an estimated 5 million adults and 1 million American adults reported using homeopathy. In 2007, out of pocket (not covered by insurance) costs for homeopathic medicines used by adults reached $2.9 billion and $170 million for visits to homeopathic practitioners.

I'm personally against the extraction method utilized by western medicine. Such as stripping a plant down to one chemical constituent to be used in a medicine. I think plants ha e grown the way they do and have been used as traditional medicines as a whole. Not to have their medicines isolated. What do you think about this? Reactionary medicines vs preventative medicines.

Monocarto

Very good concern. Plants did not grow to become medicines; they grew to survive and give rise to progeny. And the medicinal chemicals they did produce were produced to achieve that end. So I do not think that the plant as a whole is always the optimal way to develop potent treatments to diseases. Rather, they contain medicinal value that we can utilize. In the realm of antibiotics, going all the way down to one chemical constituent has the disadvantage of being very easy for the bacteria to develop resistance against it. Perhaps this can be thought of as science's first attempt to understand and utilize the complexity of natural products (this was first done with penicillin only about 80 years ago). Medicinal plants contain multiple medicinally active chemicals -- that does not mean that all the chemicals in a plant are medicinally active. In our lab we work to identify as many medicinally active chemicals in a plant as possible, and we have projects where we seek to test them in combination to identify the most efficacious combinations.

Are the antibiotics fed to the animals we consume (meat industry) bad for the effectiveness of the antibiotics used in medicine? If so how bad are we talking?

P0SWHALE

Yes. This is a huge problem. We need to stop the irresponsible practice of feeding meat animals low doses of antibiotics as growth promoters. Antibiotics for veterinary care is another matter - if an animal is sick, we need to give it proper veterinary care.

Here is a link to a new book coming out soon, which addresses this specific issue of antibiotics in agriculture: http://marynmckenna.com/new-book/

Why does the use of plant-based medicine not create resistance problems while other pharmaceuticals do?

TheThirdTesticle

The statement that plant-based medicine does not lead to antibiotic resistance is not true. However, there is an important consideration here: it is far easier for bacteria to develop resistance to a single treatment (i.e. treatment with one chemical/drug) than to a combination treatment. When a plant is used in traditional medicinal remedies, the whole plant part or a crude extract thereof is used, and so all the medicinally active chemicals in it act in concert. In this case, resistance is not observed to develop in the bacteria. However, if a purification was done on a plant extract and a single medicinally active chemical was isolated -- if that was used to treat an infection, there is a much higher chance for the development of resistance. In this case the bacterial population has only one entity to adapt to, and so the probability of resistance arising is relatively high. These statements on drug combinations vs. single drugs are true not just with natural products, but in general. Artemisinin is a natural product anti-malarial that, due in part to widespread availability of oral artemisinin-based monotherapies, has seen resistance develop against it. In addition, repetitive low dose application of tea tree oil - which represents a more complex chemical mixture - has also been shown to result in bacteria developing resistance to it.

Hi Cassandra, thanks for stopping by.

Although the article didn't say it outright, it appears that you found a quorum-quelching compound to inhibit group behaviors in MRSA. It mentioned "stopping the communication," which I presumed to be referring to quorum sensing.

My questions are: How does the quorum-quelching compounds you found not interfere with the native flora (including "standard" *S. aureus*) present on our skin, and what is the likelihood that a synthetic version of this compound being made more efficiently than extracting and purifying the wild type? If a synthetic is less efficient to produce, how would you suggest production of the qq compound through the plant?

AndrewFlash

Yes, the Schinus terebinthifolia extract acts as a quorum-quencher that inhibits the group behavior of MRSA. It works by inhibiting the agr pathway and not inhibiting the growth of the bacteria. The extract was tested against several skin microflora (P. acnes, C. amycolatum, M. luteus, etc) and was found to be nontoxic to these commensal bacteria.

It may be possible to synthesize the active compounds, but further research would be necessary. And depending on the difficulty of the synthesis it may be more efficient to isolate from the plant - or to pursue approval as a refined mixture via the botanical drug pathway.

Hi Cassandra. You may have already answered this, but what's the latest you know of possible botanical ways for dealing with drug-resistant gonorrhea? Has anyone made any progress in this regard?

Thank you so much for doing this, thank you for your time, thank you for your fantastic work for the future of mankind, and of course thank you if you ever get around to answering this. If nothing else, I wish you all the luck in the world in all your endeavors!

Chrisischan

Great question. Yes, we are facing a serious challenge in addressing MDR gonorrhea - the WHO recently highlighted this as a high priority pathogen (http://www.who.int/mediacentre/news/releases/2017/bacteria-antibiotics-needed/en/). We're not currently exploring activities of our extracts against this pathogen, and I'm not personally aware of any other natural products folks working on this. It is definitely something that could be relevant to explore in the future with the right collaborators on board (and necessary funding).

Just curious if you've worked at all with bitter melon. The Filipinos and Pacific islanders seemed to love the stuff. Claim it cleanses the blood and gives men....erm....male prowess.

I've eaten it several times and did notice an effect. I realize it's not in an infectious disease baliwick, but thought I'd throw that out there.

Not_Rocks_Marie

Hi! Thanks - I wasn't aware of these effects - very interesting. We are interested in it due to its use in postpartum medicinal food applications. It is one of more than 400 species under research in my lab.

Hi Cassandra,

I was a HPTLC Chemist at one of the best 3rd party contract testing laboratories that performed Qualitative analysis on botanical materials used in finished products or identified botanical crude powders and extracts.

I'm unsure if you're familiar with HPTLC... But I was curious on the effects of botanicals grown in different regions of the world and even altitude where they are procured. I know from experience from testing via HPTLC and even the way some botanicals are classified i.e. Vaccinium angustifolium and Vaccinium corybosum and other various blueberries, they produce somewhat different chromatograms via HPTLC, although I'm unsure about results via genetics.

Does the region/location/altitude of botanical ingredients have an effect on the efficacy of a treatment?

shekking

Many environmental conditions can influence the chemistry a plant produces. See some of the

comments in my earlier answer.
https://www.reddit.com/r/science/comments/69e7ni/science_ama_series_im_cassandra_quave_a_medical/dh6aghh/

It sounds like antibiotic resistance is more of your forte, but as a virologist, I'm curious if there is any potential for finding antiviral treatments in traditional medicines as well?

J-Nastee

Yes - there is absolutely some potential for discovery of novel anti-viral agents from plant natural products. We have done some preliminary work with Emory collaborators on high priority antiviral targets and have had some success. This work is still in progress and we hope to submit for publication this year.

Forgive my cynicism but I'm a little skeptical about progress with natural products. Do you have any opinions on these bones of contention?

-Too many poor in vitro experiments claiming extract X from plant Y 'kills cancer'...and yet I don't see anything new entering clinical use.

-The same old essential oils coming up again and again. The rest of the products can't be extracted/purified. Diminishing returns.

-The intellectual problem of a potential therapeutic effect as a natural mixture compared to science's need to purify/assay individual components.

Echo_are_one

Very thoughtful points of concern! There is no shortage of papers that perform just a few experiments, some poorly designed, and overanalyze the results. At the same time, there are many papers that properly show how extract X from plant Y does indeed demonstrate potential for drug development against cancer Z. One thing to note is that these initial stages of natural product drug development are inexpensive, and laboratories all over the world are engaged in this. After extract X has been identified, it must be developed (fractionated) further to arrive at a purer subset of medicinally active chemicals. This more sophisticated development becomes very difficult, and not many laboratories are engaged in this process compared to the amount of extracts being identified as promising. And so little tends to happen after extract X is identified. As for purifying single medicinally active compounds, it is a difficult process and requires very expensive instrumentation and highly experienced scientists.

Finally, the FDA has focused on single compounds as therapeutics due to the fact that single compounds (compound = chemical) can be highly effective as treatments and that studying just one compound is already complicated enough. In the process of pre-clinical drug development, pharmacologists must study both what the drug does to the body (eg: therapeutic effect, side effects, therapeutic window, duration of action) and what the body does to the drug (eg: how the drug is absorbed, distributed in the body, metabolized, excreted). To get an idea of how laborious this is, consider the fact that a drug is broken down (metabolized) into several different products. These must be identified and studied to understand how they are formed, when they are formed, how fast, etc and what effects these metabolic products exert on their own. That itself is an enormous undertaking, and it's only one of the many components of pre-clinical drug development, some of which I've enumerated above in parentheses. Recognition is beginning to emerge, however, that drug combinations may be superior in many cases than single drugs. For example, many cancer drugs have been found to act synergistically when given in combination. Also, the FDA's botanical drug pathway approved their first drug, Veregen, in the mid-2000s (Veregen is a specific water extract of green tea leaves from Camellia sinensis composed of multiple compounds, for topical application to anogenital warts). They also recently approved Crofelemer (from Croton lechleri) for HIV-related diarrhea. Our lab plans to submit our findings of highly active purified plant extracts to this same FDA pathway.

Don't know if this is an appropriate question. But what did you study for that field ? As in what major and minors ?

Alpha_Saturnine

I was a Biology and Anthropology major, but also premed in college (so I had a heavy chemistry background as well - organic, biochem, etc). My PhD is in Biology.

My wife has her undergrad in Ethnobotany and is now getting her MS. With your experience, what are

a few career or academic paths you'd recommend?

This AMA made my day; it was the first time I saw "ethnobotany" trend in a post!

TeacherHeze

That's great! Tell your wife to keep up the great work! In addition to academic career paths, I think that there are so many ways that ethnobotanists can make a big positive impact on the world! Because of their training across biology and anthropology, they are uniquely suited especially to contribute to development projects with NGOs, public health initiatives, conservation activities, biodiversity survey jobs, and so on. I'd even argue that we need more ethnobotanists engaged in city planning activities! Can you imagine cities filled with useful (food bearing or medicinal plants) rather than exotic ornamentals with no utility other than their beauty? We could also benefit from ethnobotanists engaged in public education! We need to teach children the value of nature, how to connect to it, and where their food comes from!

Lastly, I'd also encourage her to connect with other students in the field. The Society for Economic Botany has an active student group and a really great blog to check out: https://sebstudentblog.com/

How do you see ethnobotany responding to deforestation and climate change? From what I understand, many of the plants we get medicine from are found in select parts of the Amazon and are at risk of not being commercially available. Do you think we'll shift towards trying to find benefits in more common plants, like the invasive peppertree you mentioned, or will some of these medicines simply be lost without proper replacements?

samschurk

I think that ethnobotany can be used as an important tool to support conservation efforts in the face of mass deforestation and climate change. Check out the work underway by the Amazon Conservation Team - they have established a great model working in close collaboration with local indigenous communities to both save the land and the traditional knowledge tied to the people and the land: http://www.amazonteam.org/

What does a typical day look like for you?

KT_1497

This is a great question. In short.... the answer is "very busy" ;)

Here is a sneak peak at an unedited blurb I recently wrote for my book. It covers a typical Monday for me: http://etnobotanica.us/wp-content/uploads/2017/05/Lab-life_Monday.pdf

Can't you just perform numerical simulation of what the molecule should be to fight a specific bacteria ? Is it too complicated to be solved analytically instead of empirically ? Also do you have an opinion on bacteriophage virus as a replacement or complementary to antibiotics ?

IdoLIKEbluePOT

I wouldn't call it a numerical simulation; rather, I would call it a molecular dynamics (MD) simulation. Of course, MD is based off of equations to define physical parameters that model the biology and chemistry of a system of interest. MD is a form of rational drug design where scientists use the knowledge of a disease target as the basis for developing a therapeutic. It must be understood that treatments usually take the form of a single chemical (also called a drug) that has an intrinsic ability to bind very well to a biological target, usually a protein (proteins can be thought of as the machinery of the cell, responsible for carrying out process necessary for survival, like breaking down sugars into energy, moving the cell, etc).

For example, it may be that a person has a certain disease -- like chronic inflammation -- because one of the proteins in the cells of the inflamed organ is overactive. So in MD, a scientist would build a model that simulates this overactive protein, and then model how different chemicals would interact with it. They would look for chemicals that bind to it very well, and shut it off as a result (due to induced conformational changes in the protein structure). Or, if the scientists identify a region on the protein that is responsible for keeping it on or off, they could use MD to actually build a pharmacophore model of what types of chemicals would be best able to bind in that spot, thus shutting it off.

While final conclusions cannot be drawn just from these predictions, they are extremely helpful in informing scientists on what experiments to perform or what chemicals are most promising to look into.

While biological responses to medicinal treatments can also be modeled, these models must be bolstered by actual experimental findings to confirm their credibility. As such, molecular simulations represent a key tool in drug discovery.

Finally, I am not up to date on the field of therapeutic bacteriophage viruses

I've recently become interested in learning to draw various plant specimens. Can you recommend a good online source for viewing photographs of plants by geographic region?

Jericrich

I don't know of any online resources, but I'd encourage you to reach out to your local botanic garden. Sometimes they offer courses on botanical illustrations - lots of fun!

Wow, Brazilian pepper trees are super invasive in L.A. So much so that CalIPC lists them as a noxious, invasive weed with a "do not plant" warning, so we don't even stock them at our nursery anymore.

Given your findings, should we be reconsidering our ban and have Schinus terebinthifolius or Schinus molle available for retail at our store in particular or S. California in general?

dicot

States have these laws in place for a reason - including the protection of native species. Isn't it fascinating though how a species can be highly valued as a medicine in one part of the world and loathed as a pest in another? My next goal in the development of this technology is to start work on formulation of the extract (which is different from a simple crude extract - it is highly chemically refined and vetted via bioactivity quality control studies). My hope is to find the funding to advance this towards filing an IND (investigational new drug) application under the FDA's Botanical Drug Pathway (https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM458484.pdf) so that we can pursue clinical trials for its safe and efficacious use in treating MRSA infection.

Hello thank you for answering questions! I'm studying biology in college right now and in an intro course, we were taught the ways vaccines work. Based on your current work with treating disease, is it possible for plants to be used for the same type of purpose? Also, how long do you estimate that overuse of antibiotic treatments will start having a major impact? I know it's already starting to show up in many strains of bacteria.

navyblue161

Briefly, vaccines work by introducing a particle into a patient's systemic circulation so that the immune system recognizes it and "remembers" it. This particle would be harmless and would highly resemble part of the microbe being vaccinated against. This way, if the microbe does eventually get into your body, your immune system would be able to quickly mount a response to get rid of it because it had already seen it before. Plants could not be used for this purpose because they do not endogenously contain random particles from human-relevant pathogenic microbes. What they do contain, which the field of pharmacognosy capitalizes on, is secondary metabolites. Secondary metabolites are chemicals produced by plants that are not directly necessary for survival but aid in self defense, such as chemicals that repel insects, attract pollinators, kill bacteria, etc. Due to this adaptation, plants represent highly diverse libraries of medicinal chemicals. These libraries are still largely untapped in the field of drug discovery. As for your second question -- we are already facing a serious situation concerning antimicrobial resistance. According to the O'Neil report, 700,000 people die each year from antimicrobial resistant infections - and this is projected to reach 10 million by the year 2050 (https://amr-review.org/). We need action now.

Are antioxidant ingredients said to be in certain fruits really help our health?

RedditBadga

The short answer is maybe and it depends on which aspect of health you are asking about. In general antioxidants can act as "sacrificial molecules" to prevent oxidative damage to DNA and other important biomolecules in our cells. This can prevent damage and mutation to DNA. However, our cells also contain mechanisms to repair damaged DNA and detect and recycle other damaged biomolecules. So the cells are capable of dealing with normal levels of damage. There is certainly nothing wrong with minimizing the amount of damage occurring by eating more antioxidant containing fruits and vegetables (dark fruits - like blackberries and blueberries are a great way to boost your levels of

exogenous antioxidants in the diet). There are many studies for specific diseases showing antioxidants can be helpful in treating or reducing the symptoms including inflammatory bowel disease (https://www.ncbi.nlm.nih.gov/pubmed/28465632), certain prostate and other cancers cancers (https://www.ncbi.nlm.nih.gov/pubmed/28440320,

What do you view as the largest threat to the effectiveness of antibiotics?

For instance the overprescribing of antibiotics? The use of antibiotics in livestock production? Just a matter of time due to evolutionary conditions of the bacteria?
Or other scary stuff I don't understand ?

Thanks

ardentDuel

I think that one of the largest threats concerns our reckless use of antibiotics in agriculture - especially in meat production. By giving animals low doses of antibiotics as growth promoters, we are essentially creating a perfect storm for the creation of antibiotic resistant strains. We must also note that antibiotic resistance genes are also ancient and have been identified even in the permafrost. We are engaged in an evolutionary battle with pathogens - perhaps we need to start thinking seriously about new approaches to complement our existing arsenal (e.g., drugs that re-sensitize bacteria to antibiotics, biofilm inhibitors, virulence blockers, host-directed therapies, and etc)