Hi Reddit, I'm Debasish Bandyopadhyay of the University of Texas Rio Grande Valley. Ask me anything about natural products, organic medicinal chemistry, and drug discovery (synthetic and natural) following greener routes.

AmerChemSocietyAMA [1] and r/Science AMAs[1]

[1]Affiliation not available

April 17, 2023

the WINNOWER

REDDIT

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Hi Debasish and thank you for doing this AMA.

- I am a bit confused by the scope of your research - are you excited because you can find and purify compounds like heptacosane and docosanol from a naturally occuring waste product or are you excited because you think the avocado pit itself may represent a source of untapped, naturally occurring compounds that may have medical use? In the first case, it would be compounds that can be made synthetically, but using avocado, purified more "green-ly". In the second case, it would be the avocado pit contains novel compounds that will potentially represent new advances in medicinal chemistry.
- Why the avocado?
- How do you plan to bridge the gap from medicinal chemistry to drug development?

SirT6

Thanks for your interest in our research. As you know, the random removal of food wastes is one of the major environmental hazards around the globe. Annually about 15 million metric tons of foods are wasted in the U.S. and 1.6 billion metric tons around the world. Increasing efforts are continuing to utilize these foodstuff and related wastes in appropriate manner. Avocado (Persea americana) is a widely used healthy vegetable (fruit) that contains a comparatively big seed. In all, nearly 5 million tons of avocados are produced worldwide annually. Americans consume almost 1.9 billion pounds each year, according to the Hass Avocado Board. In most cases, the "meat," or flesh, is eaten and the seed is tossed in the trash. Some edible oil manufacturers extract avocado oil from the seeds, but they remove the husk surrounding the seed and discard it before processing. Taken together, the husk is 'waste of wastes". I mean industrial waste (husk) of household waste (seed). We, the people from South Texas, consume lot of avocados every day. The huge amount of 'waste' that is being created, actually drew our attention to avocado. We are excited because this is the first time (as per available literature) a research group has had paid attention to this 'waste of waste' and disclosed the presence of medicinally important and industrially privileged compounds in avocado seed husk. Our research indicates that if appropriate plan is taken, these valuable compounds can be isolated successfully.

Regarding your second query, we have isolated a few more compounds where there is enough scope of further functionalization. Extensive docking/molecular dynamics studies can be planned to increase the potency of these compounds. I am sure that you are aware that chemical modification of natural products leading to the synthesis of pharmaceuticals is an emerging field in drug discovery research. Please follow the below link for further info. https://www.youtube.com/watch?v=lk4tGt9aFL4&list=PLLG7h7fPoH8IE5bjJfnxCxLRCd1ggBt1X&index=7

To me, the greatest hindrance to the development of natural products, organic medicinal chemistry, and all, is the prevalence of phoneys and charlatans spreading misinformation for profit purposes. Nowadays, especially because of internet, there is a lot of shenanigans, trends, or whatever, as well as unverified and unscientific claims. People can read anything, and its contrary. And people can be very

gullible and can get taken advantage of. It's the same on the telly, with programs selling magic nutrition pills, health methods, whatever.

As a scientist, what do you think about all that? How does this affect your research? What are the necessary steps to "shut down all the shenanigans"? How to educate people? What do you think about all the pseudoscience, such as homeopathy? Or whatever comment(s) my posts inspire you :)

Thanks!

GrahamTheRabbit

First of all, you are absolutely correct. I do agree with you. This shenanigans must be STOPPED. Being a scientist, we can aware the people (may the through social media) about this potential threat. People should check/search the scientific literature before consuming any 'healthy' pills or 'tonics'.

On the other hand, global policy should me made and all the governments should keep an eye on this malpractice. There must be "sensor board" in each country who will validate all such advertisements (claims) before publishing. Any such shenanigans must be punished appropriately. The bottom line is that we can aware our real and virtual societies as much as possible.

Hello Dr. Deb! I had you for organic chemistry and you were the best, I wish you had talked about your research in class!

1. I know the RGV has a history and culture of herbal medicine, Do you feel there is still any value in searching for novel compounds in plants used for traditional medicine? Or is this aspect of the field pretty much over-done?
2. Why did your lab decide to look into avocados in particular? Did you look into other food waste products besides avocados?

Thanks for doing this AMA~

TheLovelyNwt

Thank you for your kind words. I would like to dedicate my class hours in teaching that way I can successfully complete my syllabus. Also, ethically I should not 'waste' class hours by talking on our research. Whenever a student asks me aboout research, the first thing that I suggest is to check my research interests/backgrounds in SciFinder Scholar and then (if interested) the student either can come to my office during office hours or can make an appointment. You are saying that you are/were my student. In that case, probably you know that I work only 7 days in a week :) and I dedicate plenty of hours for my students.

Now come to business :) I believe there is still ENOUGH scope to conduct research on indigenous resources that are available in RGV. At least I have a list of 6 species in hand on which NO effective research has been conducted/reported yet. https://www.youtube.com/watch?v=lk4tGt9aFL4&list=PLLG7h7fPoH8IE5bjJfnxCxLRCd1ggBt1X&index=7

We, the people from South Texas, consume lot of avocados every day. The huge amount of 'waste' that is being created, actually drew our attention to avocado. We are excited because this is the first time (as per available literature) a research group has had paid attention to this 'waste of waste' and disclosed the presence of medicinally important and industrially privileged compounds in avocado seed husk. Our research indicates that if appropriate plan is taken, these valuable compounds can be isolated successfully. And yes, we are open to work in other food waste as well.

Thanks for coming to talk with us today! The word "natural" may be the most abused in the English language. Can you give us any hints on when "natural" matters in things we buy and when it doesn't?

asbruckman

Thank you Professor for your question. "Natural" products are unique to only one species or family of organisms. Based on their source (origin), natural products can be classified in the following four categories (approximate relative abundances are given in the parenthesis):

1. Plant natural products (65-75%)
2. Marine natural products (15-20%)
3. Natural products from microorganisms (10-15%)
4. Natural products from animals (<3%)

Numerous compounds are widely distributed in nature and many of these possess medicinal/biological/pharmacological activity. The utilization of natural products and/or their novel

cores, in order to discover/develop the final drug entity, is still an interesting and highly promising area of drug discovery research. Till today about 25% medicines are directly derived from nature. About 61% of new chemical entity (NCE) can be traced to a natural product origin. In certain therapeutic area, this impact is even higher. For example, about 75% of anticancer drugs and 78% of antibacterial drugs are either natural products or chemically modified natural products which are also known as semi-synthetic natural products.

Were there chemicals you discovered in nature in the course of this research that had previously only been synthesized?

drsjsmith

We have disclosed only the compounds that have been reported in the past including an antiviral drug. https://www.youtube.com/watch?v=lk4tGt9aFL4&list=PLLG7h7fPoH8IE5bjJfnxCxLRCd1ggBt1X&index=7

The research is still under progress and we have unknown compound (never been even synthesized) under active in silico and subsequent biological evaluations. The complete results will be published in due course.

Hi and thanks for joining us today!

What are other study plants on the horizon? Coffee comes to mind as producing huge amounts of waste product while containing potential beneficial compounds.

PHealthy

You are absolutely correct. There are many others around the globe. Just we need to open our eyes to look for them:)

Green chemistry is great in theory, but what incentives are there for companies to adapt to greener routes, especially with the large initial costs involved?

davofuzz

The companies can implement greener process/technique, greener solvent/catalyst, follow the route that takes shorter reaction time and atom economical. These can be done in large scale as well. For example, many industries are being using microwave reactors which is one of the well-known green techniques.
Almost all the major pharma companies use heptane instead of hexanes.

A lot of people have come to believe "natural" means safe and that medicine is never natural or safe. Can you give some examples of natural materials that actually become safer to use when processed into medicine?

giltwist

I don't believe the concept that says "natural" means safe and that medicine is never natural or safe. As you know Socrates (the great classical Greek philosopher) was sentenced to death by drinking a juice made from hemlock herbs which contain a poisonous alkaloid coniine. In fact, there are three types of biological activities of natural products: (1) Medicinal/Pharmaceutical; (2) Narcotic, and (3) toxic/poisonous. The bottom line is that ALL the natural products are NOT safe.

Regarding the last part of your question, please consider snake venom, which are animal natural products (proteins) but are used as an important ingredient to make anti venom injection.

What is your yield % by weight?

RetardsAdvocate

Please follow the link:
https://www.acs.org/content/acs/en/pressroom/newsreleases/2017/august/avocado-seed-husks-could-be-a-gold-mine-of-medicinal-and-industrial-compounds.html

Thank you for taking your time to answer our questions! I've several I hope you have the time to answer.

1)I did a project awhile back on the potential applications of fungi in this area of research and was crushed to find there was very little... Is there a reason for this?

2) How do you feel about the bacterial resistance epidemic? Are bacteriophages or other novel approaches being considered? It seems natural is our best bet.

3) With the recent interest in Cannabis in many industries from medicine to natural products, are there other "forbidden" natural substances, or plants, that you feel should also be looked into? What are your thoughts on the Cannabis industry in respects to your area of research?

Sorry for all the questions and once again Thank You for your time!

surrealabsurdity

You are most welcome. First of all, there is NO reason to say "sorry" so far we are talking science. Regarding Q#1: In natural drug development research, the process of extraction is crucial. I would recommend 'cold extraction' procedure. Also, the way of drying is important. Please try to avoid drying under the sun. Dry in dark room with plenty (couple of fans) of air. It is always safe to start with a comparatively larger amount of the dried plant portion. Please try again with a larger amount following cold extraction procedure. Regarding Q#2: Development of drug resistance is more biological than biochemical process. Search for new and novel natural drug and synthesis of next generation antibiotics is encouraged in the battle against bacteria. Q3#: I do not have required license to work on cannabis. Just like you I guess, there should be other "forbidden" natural substances.

One of the most wasteful sides of research that I've noticed is plastic waste from the infinite number of tubes, containers, and pipettes required for research. Are there any mechanisms in place or projects designed to minimize contaminated or non contaminated plastic waste?

Dat_Archon

This is currently one of the burning issues that requires appropriate attention. Scientists are working to identify microbes (bacteria) that can destroy (eat?) plastic. Extensive research is required in this field. You may be interested in the below link: https://phys.org/news/2016-03-newly-bacteria-plastic-bottles.html

I went to school at UTRGV, please tell me, are the Stripes Breakfast tacos for 99cents as good as I remember? Also, tell the stray cats on campus I send my regards.

Sleepypand672

:) God bless you.

Many of these compounds do not appear to be found in the seeds themselves.

Where do they come from then?

Suppafly

The husk contains many compounds that are not present in the seed because husk is just a cover (protector) of the seed. The husk not only contains medicinally privileged compounds but also many toxic materials like Di-n-octyl phthalate (DOP), Diisononyl phthalate (DINP) etc. Obviously these compounds are formed in the plants., most probably by different mechanisms. We hypothesize that these toxic materials protect the seed (ovary) from external disturbances that way BBB protects our brain or OBB protects our eyes or placenta protects the embryos. The abundance of compounds is normally different in the various parts of a plant. It is very possible that the compounds that are present in the leaf might not be present in the bark. Taken together, different parts of a plant are enriched in different compounds.

Are any of the husk compounds found in the seed also? (You say many are not) Is the actual avocado seed itself a significant source of nutrition? I make salads and cook with avocado oil. I read that it has a desirable omega ratio.

screamphilling

The meat or flesh portion is healthy. There is no doubt. You can make your salad and use avocado oil in cooking. Regarding the seed itself, many research has been published. A quick hit in SciFinder Scholar using 3-4 key words "Persea americana, avocado, seed" shows about 703 references. Some toxic materials might also be present.

With the thousands of uses that natural remedies have such as how Cannabis has shown to have industrial applications (hemp) to curing cancer and halting seizures (CBD oil). Why is it so difficult to persuade pharmaceutical companies to adopt more natural methods of medicating patients and industrial companies to use renewable resources in manufacturing things such as; packaging and fuel?

Mr_Reddit_User

In general, development of of a natural drug takes comparatively longer period than a synthetic drug. More patience is also required. Even after that, the utilization of natural products and/or their novel cores, in order to discover and develop the final drug entity, is still an interesting and highly promising area of drug discovery research. For example, in the area of cancer, over the time frame from around the 1940s to the end of 2014, of the 175 small molecules approved by the US Federal Drug administration (FDA) or its similar organizations worldwide. Out of these 175 small molecule anticancer drugs 131 (74.85%) are completely non-synthetic molecules. Interestingly, 85 anticancer drug molecules (48.57%) either are actually being natural products or directly derived therefrom. In other areas, the influence of natural product compounds is quite marked as well (~78%). Anti-infective area being dependent on natural products and their structures as well. The rapidly evolving recognition that a significant number of natural product drugs/leads/hits are actually produced by microbes and/or microbial interactions with the "host from whence it was isolated", and therefore it is considered that this area of natural product research should be expanded significantly. In addition, the question of total expenditure should also be considered.

As you know, antibiotics are losing the war against bacteria, slowly but surely. What are some ways you hope to find new antibiotics?

Anon9742

Because of this reason (that you have mentioned), scientists are working to develop the NEXT generation antibiotics.

Thanks for joining us today! Do you think isolating these compounds from waste produce will be more efficient (for cost, energy, and/or pollution) than generating them in traditional or synthetic ways?

p1percub

I am positive. An appropriate policy should be developed to collect the seeds. Once you have seeds in hand, the rest of the process is not difficult. Classical extraction/isolation/structure elucidation procedures need to be followed. One of the interesting aspects of Natural Product Chemistry is that it requires less money but more time and patience.

How does litmus paper or any other indicator work? Is it because of some sub-atomic particle exchange or something?

AceTrainerTundra

It depends. In some cases, due to extended conjugation. Sometimes electronic transition. Some other factors are also there.

Hi and thank you for your work, it sounds fascinating. I have an interest in Omega 3s in our food supply, but currently, the best sources of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are cold water fish and some algae. I'm curious if you know of any sources higher in EPA to DHA outside of cold water fish? In recent years some algae have been produced to contain both EPA and DHA, however, the EPA is typically low. For sustainability, and environmental reasons outside of fish, curious if you have any other sources?

anotherpinkpanther

Thank you for your encouraging words. So far I know still cold water fish and some algae are the potential sources of EPA and DHA.

What's your take on naturally extracted SSRI isotopes extracted from brains of other mammals for human supplementation/psychotherapy use?

Ferragho

More research is required before coming to a conclusion.

Thank you for shedding light on the industrial/medicinal value of biomass.

In your view, would investments in plant based petroleum alternatives generate a viable feedstock over the next decade? Cellulosic ethanol, isobutanol, alternative plastics, new analgesics(dextro-delta-9-THC), etc are coming online at a rapid pace. How do we attract more interest in supporting this methodology?

Infinitopolis

So far, the materials are eco-friendly and cause less hazards they are acceptable. I guess someone from business world can give you a better answer.

People often talk of THC or Marijuana being a near non-dangerous drug, at least compared to alcohol, mdma and other soft drugs. One notion for this is it's solely psychological addiction potential.

If it's addictive qualities are solely psychological what is the origin of universal and physiological withdrawal symptoms?

hans-georg

It is an interesting question and many people ask about this. I believe extensive translational research is required to address the question more appropriately.

I used to live in New Mexico and the Mescalero Apache would harvest Osha root (Ligusticum porteri) which is great for sore throat and acts as a bronchial dialator. However, there is a challenge in cultivating it because of it's narrow growing conditions and dependence on mycorrhizal fungi. What common challenges like this need to be overcome in order to follow greener routes in medicine?

twofedoras

First of all, the procedure must comply the 12 principles of green chemistry as much as possible. please follow the link: https://www.acs.org/content/acs/en/greenchemistry/what-is-green-chemistry/principles/12-principles-of-green-chemistry.html

Then additional requirements that have have developed lately like In the case of atom economy (AE) the efficiency of a reaction is measured by the number of atoms in the reactants which appear in the final product. AE was purposefully designed to be very simple to implement and interpret, therefore a number of assumptions have been made. AE assumes both 100% yield and stoichiometric loading. It is however, an excellent metric to assess how efficiently a reaction has been designed with respect to the utilization of reactants and was included in the toolkit for this reason. It was also deemed useful to consider AE alongside another metric, reaction mass efficiency (RME). As we know: % Atom Economy (AE) = (FW of the desired product/FW of all reactants) X 100 RME (reaction mass efficiency) = (Mass of isolated product/ total mass of the reactant) X 100

Both RME and AE are ideal for analysis of screening results as the mass balance of data, which would be directly scalable, is considered (e RME provides a fuller picture of the utilization of reactants. As RME is mass based, it incorporates yield and stoichiometry in addition to AE. As such AE gives the theoretical maximum efficiency of reactant utilization, while RME gives the observed. Comparison of the two gives a new metric, optimum efficiency (OE). OE = (RME/AE) X 100

The inclusion of OE allows for direct comparison of different reaction types which is not always possible with AE or RME as certain types of chemistries are intrinsically atom or mass efficient, while others are not.

As yield, AE and RME only provide information about the efficiency of the reaction in terms of the reactants, it should be used in conjunction with other mass based metrics. [My question: is it related to process chemistry?]. Mass intensity = Total mass in a process or process step/ Mass of product

This important metric captures all mass based inputs, such as solvents, catalysts, reagents, work up

etc. in addition to yield and stoichiometry and is referred to as mass intensity (MI) for a single step or process mass intensity (PMI) for an entire process. Improvements in the metrics are easier to follow if data can be separated out, for example giving a PMI breakdown for 'chemicals' (reactants, reagents and catalysts), PMI for solvents and PMI for workup, as well as a total figure. If used in conjunction with a bill of materials, simple manipulation of the top line of the equation allows assessment of the impact of each input class and as such indicates where greatest efficiency gains can be made. This is one of the reasons that the pharmaceutical industry view MI/PMI as the most important mass based metric. Additionally, when looking at a synthetic route of more than one step it is useful to examine metrics both stepwise and cumulatively.

A bit offtopic, but have you ever eaten a fruit/veggie smoothie that contained an avocado pit (blends nicely) ? And do you see any serious risks with it*?

dumnezero

It is NOT safer to try it.

What drug is the next Taxol? By that I mean do we have any phytochemicals on the market that still need to by synthesized in large amounts or do we have that covered now?

Murdock07

The battle against cancers is still ongoing although taxol is in the market. As you know based on cell/tissue types there are more than 400 different types of cancer are known. Accordingly, search for new drugs with more potency and less toxicity (toward normal cell/tissue) are always continuing.

Go Vaqueros! I've been on the same research grants with one of your students!

anyways my question for you is, 300 avocado's worth of stuff sounds like a lot compared to what you can yield.

Is there a plan to make the collection of the husks easier? Like can you partner up with restaurants or plantations?

What made you choose avocados? Is there any other plant/seed/fruit/vegetable that you also looked into?

theevilhillbilly

Gracias.... To answer your first two questions an appropriate policy should be developed. May be the business people can provide better suggestion. Regarding last two questions: The people from South Texas, consume lot of avocados every day. The huge amount of 'waste' that is being created, actually drew our attention to avocado. We are excited because this is the first time (as per available literature) a research group has had paid attention to this 'waste of waste' and disclosed the presence of medicinally important and industrially privileged compounds in avocado seed husk. Our research indicates that if appropriate plan is taken, these valuable compounds can be isolated successfully. And yes, RGV is rich with its indigenous plants.

Are you sure that the phthalates and BHT actually came from the avocado? Couldn't they be contamination?

-Metacelsus-

Absolutely sure. There is no question of contamination.

From a technical perspective, was there anything interesting or unusual you had to do to carry out the MS runs and analysis, or was it fairly routine?

JohnThePhysicist

It was fairly routine.

While watching your press conference I was wondering why an avocado may make these chemicals,

and my guess was that they served as antimicrobial or antiparasitic defense, so I'm glad that I was barking up the right tree!

I studied pharmaceutical science for my BSc and I really enjoyed my medicinal chemistry lectures and, as someone with strong environmentalist values, I also have a personal interest in natural product discovery. Do you worry that climate change and environmental destruction could be causing us to lose potential holy-grail drugs forever? And do you know of any conservation efforts being made with a NPD focus?

And for a more personal query: I didn't find my analytical chemistry lectures that interesting, and working in a couple of analytical CROs since then has done nothing to change that (although this could be more due to working in a private/industry setting. I love learning and experimenting, but there's few no-no's bigger in a GMP lab). Are there roles for someone who is interested in NPD but would rather stay out of the lab, particularly in academic research?

Thank you!

panmorphic

1st paragraph: It is good to know that we are on the same page 2nd paragraph: You are absolutely correct. Every year many species are being enrolled as 'endangered' and many species are becoming extinct because of global warming and related issues caused by this. A few initiatives are underway. Please check the US-environmental protection agency website for more info. 3rd paragraph: I believe will power is very important in research. If someone has keen interest, there must be way. You can work on chemical modification of natural product (in silico) by extensive docking studies and/or molecular dynamics study using your computer from outside the lab. As you know many commercial drugs are chemically modified natural products and this is an emerging area of drug discovery research nowadays. You can contact any potential lab that is involved in natural drug development and contribute in silico part from your home.

What is the best natural solution currently to ADD/ADHD?

Rainseeker777

People say 'yoga' is the best solution but I am not sure. Please talk to your doctor.