THE VORTEX

The American Chemical Society
California Section Newsletter

May 2023, Volume 85, Issue 5

WHAT'S INSIDE

Meetings, Activities, and News

History and Education

The Vortex is published monthly except July and August by the California Section, American Chemical Society. Opinions expressed by the editors or contributors to *THE VORTEX* do not necessarily reflect the official position of the Section. The publisher reserves the right to reject copy submitted. Subscription included in the annual dues payment.

MAGAZINE OF THE CALIFORNIA SECTION, AMERICAN CHEMICAL SOCIETY

Editor:
Donald MacLean
Donald.maclean.acs@gmail.com

Article Contributors:
Nicki Davis
William Motzer

Office Administrator Manager:
Julie Mason
2950 Merced St. #225
San Leandro, CA 94577
510-351-9922
office@calacs.org
web site: http://www.calacs.org

Editorial Staff:
Outreach: Alex Madonik
Editorial Assistants: Jim Postma and Linda Wraxall
Web Page Posting and Editor: Donald MacLean or Alex Madonik

Cover Photo Credits:

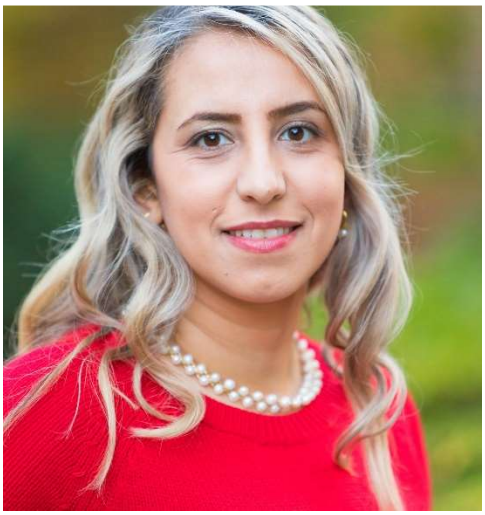
Top Left: Speaker – WCC Flyer
Middle Right: Speaker – WCC Flyer
Middle Left: Grass in Bloom – Donald MacLean

If you have material you think is worthy, submit it to Donald.maclean.acs@gmail.com

This month's focus was to be on our volunteers who were / are veterans. As of this moment only 3 people have come forward, one of which did not want to publicize his time. I also share the same feeling about not publicizing my service time as I feel I cannot compare my time with some who did their time, and general support for the military in our section area is not as strong as other focus areas such as the Earth Day, Education, and Diversity and Inclusion topics.

To supplement our intended focus, I decided to add a bit of trivia for the 7% of the US population who have performed military service in some form, active, reserve, or ROTC. This will include 2 services that are not an armed component of the Uniformed Services, but still wear the uniform when performing their duties in a war zone, which grants them prisoner of war (POW) status if captured.

Chair Message - Atefeh Taheri



Greetings and welcome to the May edition of Vortex. As we enter the fifth month of the year, we would like to take a moment to recognize and thank our veterans, as May is Military Appreciation Month in the United States. We are honored to have members of our section who have served our country, and we express our deepest gratitude to all veterans and military personnel for their service and sacrifice.

In this edition of Vortex, we feature the profiles of a few of our section volunteers who have served our country, and we commend them for their dedication and commitment to our country's defense. We are grateful for their selflessness and their contribution to making our country a better place to live.

April was a busy month for our section volunteers, who led two successful events. The first event was the Earth Day Celebration at the John Muir National Historic Site in Martinez, CA. Our volunteers showcased hands-on chemistry activities related to the 2023 Earth Week theme, "The Curious Chemistry of Amazing Algae". We appreciate the engagement of attendees, especially the children who were excited about the experiments. The second event was the 2023 Chemistry Olympiad. You can read about it on Page 7.

As we celebrate Mother's Day on May 14th, we also take the time to acknowledge and appreciate all the fantastic moms out there. In honor of this special day, we invite you to read this 2014 article titled "Mother's Day Science: Reactions Highlights Amazing Facts About Pregnancy." This article explores the incredible science behind pregnancy and the role of chemistry in understanding this complex process.

Thank you for your continued support of the California Section of the American Chemical Society. We hope you enjoy this month's edition of Vortex and look forward to sharing more exciting news and events with you in the months ahead.

https://www.acs.org/pressroom/newsreleases/2014/may/mothers-day-science-reactions-highlights-amazing-facts-about-pregnancy-video.html

Upcoming Events

Julie Mason

1. Sat. May 6th, 8:30 am – 12:30 pm., Northern California ACS Undergraduate Research Symposium St. Mary's College. See calacs.org website for details. Encourage your students to submit an abstract by the April 24, 2023 deadline. For more details contact Steven Bachofer at bachofer@stmary-ca.edu. Please include NorCal Undergraduate Symposium on the subject line.

2. Sat. May 13th, 1:00 p.m., Zoom, Building a competitive and multi-facetted research portfolio: an outsider's perspective, Sudip Das, PhD

3. Sat. May 20th, 11:00 a.m., Zoom, Biomedical scientists making their mark in clinical research: Experience on a journey without a map, Rajan Singh, PhD

4. Awards Luncheon, date and location to be determined.

California Section
American Chemical Society

Women CHEMISTS Committee

All are welcome
Saturday, May 13, 2023

Title

Building a competitive and multi-facetted research portfolio: an outsider's perspective

Time

10:30 – 11:00 am
Chatting

11:00 am
Talk and Discussion

Reservation

Please visit the CalACS website www.calacs.org to register for this meeting or use Brown Paper Tickets.

RSVP here!

Please register before Thursday, May 11, 2023, 12 noon. Your email address is needed to send the ZOOM link, which will be shared with attendees on or before the day of the event via Brown Paper Tickets.

Cost

Free!

About the Speaker

Sudip Das, PhD

Born in the city of joy, Kolkata, India, Sudip's early life was urban and cosmopolitan with an upbringing including several languages, cultures and perspectives. Sudip studied Bachelors at Utkal University and Masters at KIIT University in India. For his Master's research, he received the Swiss Academy of Sciences Fellowship to go the prestigious ETH Zürich, Switzerland, where he worked on Salmonella infections. Fascinated by the research and life in Europe, Sudip obtained his doctoral degree *summa cum laude* in human bacterial infection of the lung and blood from the esteemed University of Wuerzburg in Germany. During his PhD, he was awarded multiple fellowships including DAAD and awards like Biocenter Science Award. He personally has always focused on acquiring new skills. Following his newfound interest in computational biology, he moved back to Switzerland with the prestigious Marie-Curie fellowship for postdoc at the University of Lausanne. Here, he combined conventional microbiology with computational biology to become a dual-expert. Since June last year, Sudip is a Research Group Leader at the University Hospital Bern, Switzerland, where he is laying foundation for the first lab nation-wide dedicated to comprehensive human lung microbiota research. In addition, he is an evaluator for European Union Horizon research grants and reviewer for prestigious publication houses like Springer-Nature, Elsevier, American Society of Microbiology, PLoS etc. He's a big proponent of Women in STEM and has mentored several female scientists throughout his career.

Abstract

Why an outsider? The reason is that in all aspects of life: research, social life or acquiring new skills, I have always stepped out of my comfort zone and placed myself as an outsider. Even for this talk where all of us are scientists (budding, active, career seeking, or retired), I will address an audience of different genders on a different continent. I will talk about my research, how to build multiple expertise and women in STEM. This will include my personal experiences and how I integrate the correct form of diversity of minds and perspectives. I will not only share my journey as an outsider furthering my career and contributions of my peers throughout, but also give you insights on research and life at my home base in Europe.

Questions?

Please contact Elaine Yamaguchi at eyamaguchi08@gmail.com

California Section
American Chemical Society

Women CHEMISTS Committee

All are welcome

Saturday, May 20, 2023

Title

Biomedical scientists making their mark in clinical research: Experience on a journey without a map

Time

10:30 – 11:00 am
Chatting

11:00 am
Talk and Discussion

Reservation

Please visit the CalACS website www.calacs.org to register for this meeting or use Brown Paper Tickets.

RSVP here!

Please register before Thursday, May 18, 2023, 12 noon. Your email address is needed to send the ZOOM link, which will be shared with attendees on or before the day of the event via Brown Paper Tickets.

Cost

Free!

About the Speaker

Rajan Singh, PhD

Rajan Singh was born and raised in India, a developing country with diverse cultures, religions, traditions, and languages, all nearby his home. Thus, he appreciated diversity from a young age. After obtaining his BS in Biological Sciences in 2007 from the University of Lucknow, he enrolled in a doctoral program at Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGIMS), Lucknow, one of the best medical schools in India. After gaining extensive experience and knowledge in the gastrointestinal (GI) motility field during his doctoral studies, he did postdoctoral research in the same field by joining the lab of Professors Seungil Ro and Kent Sanders, leaders in the field of Gut Motility Research. From 2021, Rajan became an Assistant Professor (Research), Department of Physiology and Cell Biology, School of Medicine, University of Nevada, Reno, USA. He has mentored first-generation graduate students and fueled their aspirations to become successful academicians by training them with adequate skill sets and future research goals/perspectives.

Abstract

Life is full of challenges at each stage. Rajan will describe challenges he faced from his graduate school career, along with the skills he developed to overcome them. Moving to the US for his postdoctoral work presented a new set of challenges with the opportunity to develop new solutions, both technical and non-technical. One of his technical contributions involved understanding the cellular and molecular defects in interstitial cells of Cajal (ICCs), and enterochromaffin (EC) cells in the pathogenesis of gut motility disorders and diabetes. He characterized gene knockout mice for gut dysmotility and diabetes. On the non-technical side, since Rajan started taking responsibility for his family members very early, he learned how important it is to cooperate and show mutual understanding and respect, which eventually produces stronger relationships. His relationship management skill was reinforced and strengthened through academic/clinical collaborations with fellow researchers. He will discuss the advances in understanding the pathogenesis and therapeutics of Gastroparesis, a disorder of Gut-Brain Interaction. In his role as research professor, he provides his students with skills needed for the modern scientific lab.

Questions?

Please contact Elaine Yamaguchi at eyamaguchi08@gmail.com

2023 CalACS Chemistry Olympiad Report

Eileen Nottoli

Our efforts to support high school students with the Olympiad start in early fall. We reach out to teachers with an email on general chemistry and Olympiad weekly tutoring by chem and chemE students at the University of California, Berkeley. About 20-30 students take advantage of the tutoring each year. Each January, we send a packet of information to every high school in our Section in January with information about the Olympiad and other programs sponsored by our Section. We follow-up with teachers interested in participating and again remind them of the tutoring.

This year, students from twenty-four schools, two home-schooled students, one student from a non-participating school, and one student at an online school contacted us on participating in the Olympiad. We sent the Local exam booklet and a scan sheet to every teacher who responded. Teachers were to proctor the exam and send us the top results and had scheduled a date to proctor homeschooled students and students at non-participating results with the online exam. As testing was about to begin at some schools, we learned about the leak. We quickly notified all participating teachers to not give the original Local exam and advised we would provide more guidance shortly.

Upon receipt of the new exam, we copied the exam and hand delivered the exam to those teachers who had scheduled the exam within the next few days and mailed the exam to those whose exams were scheduled later. We included in the exam packet a pin with a science theme for each teacher. We also proctored the students who were homeschooled or at nonparticipating schools on April 1 with ACS.

We selected and notified the top students in our Section with an invitation to participate in the National exam; one student declined because of a conflict with the Science Olympiad. Of the fourteen students that participated, one was competing for his third time, three were competing for their second time, and the other ten were taking the National exam for the first time including one sophomore. One student lived more than 75 miles from our test location and was the first recipient to take advantage of our program to reimburse such students with a travel stipend of up to $250. We had set up this program to attract students who live outside the immediate Bay Area.

The National Olympiad was held at Santa Clara University. All students were on time and we administered Parts 1 and 2 before the lunch break. After the lunch break, students went into the lab for Part 3. We met briefly to hand each student a congratulatory letter with a $50 check and an Olympiad pin of their choice as well as a California elemental pin.

In addition, four students who participated in the Olympiad were nominated by their teacher as Exceptional students and were given additional checks for $100.

[Editor Note] PS. One of the students in our Section – a junior from Mission San Jose – qualified for Study Camp! She is one of only twenty students in the US that qualified! The study camp will be at the University of Maryland at College Park.

Uniformed Services

Donald MacLean

This month's issue the focus is on those who served in the military, which is part of the Uniformed Services. Here are some interesting facts about military service and the Uniformed Services.

During World War II there were 12 million men and women in uniform when the US had a population of 140 million (8.6%). Today the US population is around 332 million with active force around 1.4 million (0.4% of the population). The reserve component can be many times larger than the active component and visa versa. It is estimated that 7+ % of the USA population have served, with that percentage decreasing since the bulk of that number came from active war periods like Vietnam and WWII.

Today 71% of youth do not qualify for military service because of obesity, drugs, physical and mental health problems, misconduct, and aptitude.[1]

79% of Army recruits had a family member who had served.

Service starts from enlistment / draft / or ROTC (Reserve Officers' Training Corps). Today there is no draft as the military is a volunteer force. However, males 18 to 25 years old are required to register for selective service. This requirement does not apply to females.

The active and reserve components intermingle at basic training and AIT (Advanced Individual Training). Members can start at the reserve component and change to active duty, or after completing their active-duty component join the reserve component. There are 4 non active-duty components (ignoring the full time component of the reserves), the service reserves (federal allegiance only), national guard (state and federal control), Individual Ready Reserve (IRR, inactive status), and state militia (state only) [editor / writer comment: This is hard to figure out as the internet information is confusing so I am going by personal experience].

A disproportionate number of military recruits come from the South. The following table shows where the top 50% come from. Some states provide lower than their share of military recruits such as California and New York.

Table 1. 2021 US Army Recruitment Stats by State.		
State	Percent Army recruits (%, if above or below % US population)	State percent of USA population[2]
Texas	12.1 above	8.7
California	9.9 below	11.8
Florida	8.5 above	6.4
Georgia	4.9 above	3.2
North Carolina	4.7 above	3.1
New York	4.6 above	6.0
Ohio	3.4 equal	3.5
Virginia	3.1 above	2.6

There are eight uniformed services. Five are traditional military branches, one is with the Homeland Security Department that becomes part of the Navy in war time, and 2 services are civilian (non-armed). Since NOAA (National Oceanic and Atmospheric Administration) and PHS (Public Health Service) may perform their duties in a war zone, they wear a modified military uniform even though they are not part of the military. A uniform grants the service member POW (Prisoner of War) rights if captured, thereby they are not treated as a spy. The PHS wears the Navy uniform in public gatherings such as expert committee meetings when they represent the FDA. The following are the 8 uniform services with the patches (Figure 1):

Figure 1. The Patches for the 8 Uniformed Services.[3]

1. Army (Regular, Reserves, National Guard)
2. Marine Corps (Regular, Reserves)
3. Navy (Regular, Reserves)
4. Air Force (Regular, Reserves, National Guard)
5. Space Force
6. Coast Guard
7. Public Health Service Commissioned Corps (covers wide area including FDA, USDA)
8. National Oceanic and Atmospheric Administration Commissioned Officer Corps (NOAA)

References:

1. https://recruiting.army.mil/pao/facts_figures/
2. https://en.wikipedia.org/wiki/List_of_U.S._states_and_territories_by_population
3. https://en.wikipedia.org/wiki/Uniformed_services_of_the_United_States

Donald MacLean

1. How long is that you been an ACS member and involved with Cal ACS?
33 y, 26 y local activity.

2. What inspired you to become involved with Cal ACS? or What do you enjoy most about volunteering with Cal ACS?
Majored in Chemistry. Volunteer activities lead to working with people with different backgrounds and focus activities.

3. Can you tell us a bit about your background and experience in the chemical industry or academia?
Series of postdocs then took an industrial protein pharmaceutical RD position in formulation and analytics.

4. What military branch did you serve in, and what were some of the most memorable experiences during your service?

National Guard and Army.

There were two lines for chow, fast food, and home cooked food. The line for hotdogs, hamburgers, pizza had twice as many people as the home cooked line. I ate using the home cooked line except on steak lunch Thursdays. What surprised me is that the food was free all you can eat, so why would you prefer hamburgers and hotdogs with French fries?

More chicken. I said “That is not chicken, the veins are too big”. They served a lot of rabbit at Fort Leonard Wood. Meals Rejected by Everyone (MRE = Meals Ready to Eat) is actually good, even the pork patty which tasted like dried dog food.

Reading material was brought down to the grade 8 level. This meant the AIT training materials were hard to read as they were too simplified, the SMART book (specific reference book to a subject) was created for dummies, and the safety pamphlets were distributed in comic book format.

Don’t touch your eyes when working with dynamite. It really causes itching that does not stop.

The military has a lot of phases with a test at the end. Each proficiency test (i.e., rifle, grenade, physical fitness) was a competition. Graduate school was structured in the same way (Qual exams, awards, publications). The better I did the less important it became and visa versa.

I believed California fell into the ocean due to an earthquake during basic training.

I never saw so many tar paper houses mixed with wealthy houses as during my service time.

We brought tear gas, batons, ballistic vests, and ammo to deal with the 1989 earthquake riots that never happened. Our formation commands were in German as these sounded more authoritarian, and we figured people did not know the language (s).

5. How has your military service influenced your work in the chemical field?

The GI bill paid for my college bills which in time lead to my chemistry degree. The time in the reserve component was a mixed bag, both a hinderance (worse grades and time doing something other than school studies) and a benefit (more financial security).

The military is a leader in social integration. You get to meet people that you otherwise would never meet in the chemical field; racial makeup, where they are from, and current occupation. The diversity cannot even come close, even in the Bay Area. To this day at work meetings I rather socialize with different silos rather than my group to find out what is going on. This has hurt my advancement as they think I am unsociable when it is actually the opposite.

Both places use a lot of acronyms that only insiders understand. The military creates alternate names for things like the unisex unitarian black glasses are known as birth control glasses / rape prevention glasses (for boys it is BC / for girls it is RPG). A lot of things get a second name and once you get that moniker, you will never get rid of it. The worst part is when you get the same moniker later with no connection between the military and civilian activities. I would never use a moniker in the real world.

The military reads initial training to you while industry refers you to do internet training at your own pace. Both are substandard techniques. I learned to document every training and put a line through after the last item, initial and date.

In the military physical fitness is important with education becoming more important as you move up. In the workplace no one cares about physical fitness. In the military awards are important, whereas in industry my society / industrial awards are viewed with skepticism, in some cases with disgust. I have stopped showing off my awards.

Being on time was always important. Each year we had a weekend where medical readiness was performed. One cold stormy weekend we were mustering in Eureka at 7 am. It was snowing and Hwy 101 was closed north of Willits. I kept driving as there were no roadblocks. I lost control on a bridge and did a 340 (I did not make it completely around) when I applied the brakes. I arrived around 6 am to a deserted Eureka. My team rolled in throughout the day. Turns out it was okay to be late under the circumstances. Lesson learned, be safe over being on time.

My first exposure to osmolality came in the shots unit at AIT. A bowl contained bottles of sterile water and 0.9% NaCl. I picked up the sterile water and indicated that to the observer. He said continue. Instead of reselecting to get 0.9% NaCl, I filled the syringe with the sterile water. When I was injected with that water, it hurt. I never forgot for two reasons, the osmolality induced pain, and fix something that is wrong. 20 years later, osmolality became one of my pharmaceutical compendial oversite topics. I use this experience to explain osmolality as pH seems to be the dominate basic test people focus on as osmol is too abstract.

I did a few IV setups and shots during my time. 20 years later, my industrial position was doing a clinical evaluation and choosing a device. I knew the clinical head did not know anything about needles and what they were for. There is nothing like arguing about the appropriateness of a 4 inch 16 gauge needle for SC (under the skin) use in a clinical study. I ended up teaching the expert head and my successor for clinical studies on what needles, and ancillary materials to use.

Lee Latimer

1. How long is that you been an ACS member and involved with Cal ACS?
52 years ACS, 23 CalACS. Before that served Silicon Valley, Philadelphia and Rochester Sections.

2. What inspired you to become involved with Cal ACS? or What do you enjoy most about volunteering with Cal ACS?
Cal ACS was closer to my home than Silicon Valley for meetings though I worked in SV. Always worked with ACS sections because I enjoyed the projects, outreach and colleagues.

3. Can you tell us a bit about your background and experience in the chemical industry or academia?
Largely industrial chemistry and pharmaceutical drug development, with some teaching at evening classes and one semester at SFSU, all in organic chemistry. Now consulting where needed by small companies.

4. What military branch did you serve in, and what were some of the most memorable experiences during your service?
No military service other than 2 years of Air Force ROTC as undergrad, though service by grandfather (WWI), father (WWII), four uncles (WWII and Korea) and a brother during Vietnam.

How Sweet It Is!
Part 3

by
Bill Motzer

Introduction: In Part 2 of this series (Motzer, 2023), I discussed some of the chemical characteristics and properties of the sugar-alcohol sweetener known as erythritol. Another dietary sugar that we tend to overlook is lactose also known as milk sugar. Lactose is the sugar that we're most in tuned to because it's the first sweetener ingested as newborn infants.

Sources: Lactose is one of the main constituents of human and most mammal (largely bovine) milk (**Table 1**). It's a slightly sweet, reducing disaccharide unique to milk composed of glucose and galactose (**Figure 1**); it acts as milk's energy-carrier. Bovine milk generally contains about 4.8% lactose; however, this amount decreases with an animal's advancing lactation and mastitic infection. Milk lactose concentrations of principal dairy species (i.e., buffalo, cow, goat, and sheep) have a narrow range at approximately 4.5% to 5.0% with little to no effect of animal's breed, individuality or nutrition on the milk's lactose content. This is due to the relationship between lactose concentration and the animal's blood fixed osmotic pressure (Fox, 2011).

Industrially manufactured lactose is used in many foods (i.e. infant formula, yogurt, ice creams), animal feeds, and pharmaceutical products. Production is from whey, a byproduct of cheesemaking and casein manufacturing, by crystallizing an oversaturated solution of whey concentrate (Johnson and Conforti, 2003). The global lactose market is projected to grow from $2.32 billion in 2022 to $3.00 billion by 2029, at a compound annual growth rate of 3.8% (Fortune Business Insights, 2022).

Chemical and Physical Properties of the Lactose Sugars:

Lactose (galactosyl-β(1→4)-glucose) has rather limited solubility (21.6% by weight at 25 C) and crystallizes readily as the monohydrate ($C_{24}H_{22}O_{11} \cdot H_2O$). It's a reducing sugar occurring as α- and β-anomers (Figure 1). Lactose's crystallization occurs from saturated solutions: at less than 93.5 C it forms α-lactose monohydrate crystals; at temperatures greater than 93.5 C anhydrous crystals of β-lactose form. When compared to other disaccharides, lactose solubility is relatively low: at 25, 40, 60, and 80 C, respectively, 22, 32, 59, and 99 g, respectively of anhydrous lactose solubilized in 100 g water. When α-lactose or β-lactose, dissolves in water, an optical rotation occurs (aka mutarotation) with interchanges of the anomeric forms occurring until, at 25 C, with an established equilibrium of 37% α-lactose and 63% β-lactose (alpha has anomeric carbon C1 -OH down, beta has C1 -OH up) (Figure 2). Lactose sweetness is about 30% that of sucrose Johnson and Conforti 2003; Gänzle, 2022).

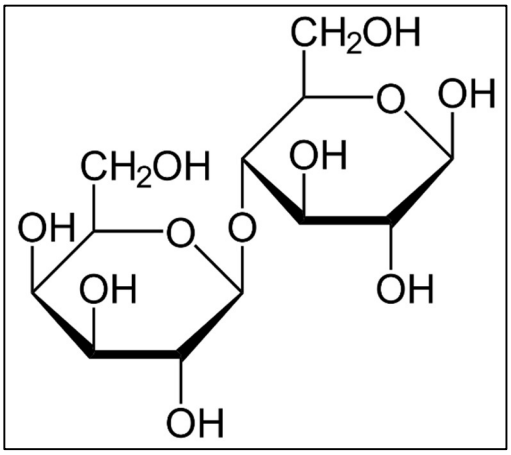


Figure 1: Haworth Projection for Beta Lactose structural diagram with beta glucose on the upper right and beta galactose on the lower left.

Glucose ($C_6H_{12}O_6$; CAS 50-99-7) also known as (aka) dextrose and grape sugar is a monosaccharide with a water solubility of 909 g/L at 25 C, a molecular mass of 180.16 g/mol, and a density of 1.54 g/cm^3 It has a melting point of 146 C (SigmaAldrich, 2023). In solid form it occurs as a white powder with a sweet taste (ILO-WHO, 2021).

Galactose ($C_6H_{12}O_6$; CAS 59-23-4) is a monosaccharide about as sweet as glucose, but only 65% as sweet as sucrose ($C_{12}H_{22}O_{11}$). It's similar to glucose in its structure, differing only in the position of one hydroxyl group. Galactose has a molecular mass of 180.16 g/mol with a density of 1.5 g/cm^3. In pure form it's occurs as an odorless white solid with a melting point ranging from 168 C to 170 C. It has a water solubility of 650 g/L at 20 C, and is an aldohexose and C-4 epimer of glucose. A galactose molecule linked with a glucose molecule forms the lactose molecule (**Figure 1**) (Williams, 2003).

Because of lactose's low solubility, crystallization behavior, and hygroscopicity, it can cause digestive problems when concentrated, dehydrated, and frozen products are ingested. Such problems are largely confined to bovine milk because very little of such products are produced from the milk of other animal species. The problem is that the digestive process requires the enzyme lactase and although lactase is readily secreted in infants, It may be diminished in adulthood. And I'll discuss lactase in the next part.

Table 1: Lactose in Selected Dairy Products

Food item	Amount (g)	Lactose (g)
Milk: skimmed, low-fat, whole	245	8.5-12.8
Lactose reduced milk	244	2.5-3.5
Nonfat dry milk	30	11.6
Cheese: cured, natural	28	0.4-0.8
Processed cheese	28	0.4-4.1
Yogurt	227	4.3-17
Butter	15	0.1
Ice cream and ice milk	99	5.5-14.5

Source: Johnson and Conforti (2003).

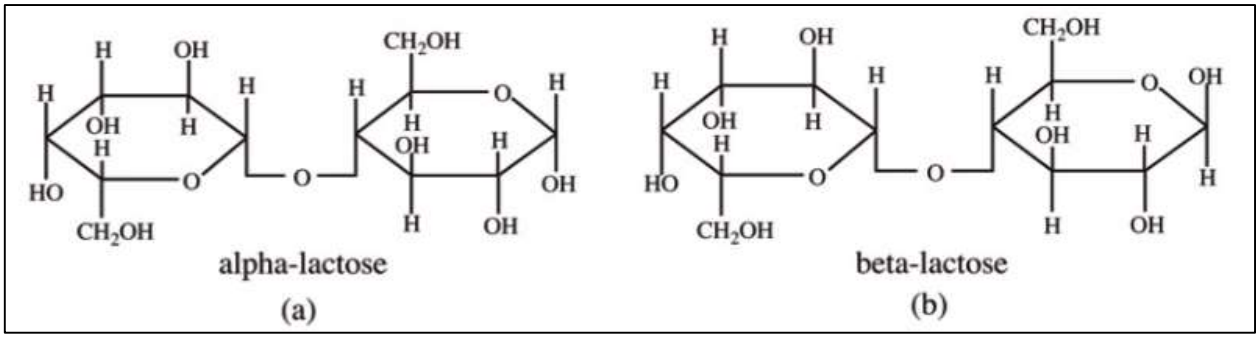


Figure 2: Chemical structure of alpha-lactose (a) and beta-lactose (b)

References:

Fortune Business Insights, *Lactose Market Size, Share & COVID-19 Impact Analysis*: https://www.fortunebusinessinsights.com/industry-reports/lactose-market-101774 (2022).

Fox, P.F., *Milk/Bovine Milk*: in J.W, Fuquay, P.F. Fox, and P.L.H. McSweeney (editors) *Encyclopedia of Dairy Sciences* (Second Edition): Academic Press (2011).

Gänzle, M.G., *Chemical and Physical Properties of Lactose*: in L.H. McSweeney and J. P, McNamara (editors) *Encyclopedia of Dairy Sciences (Third Edition)*, Academic Press (2022).

Goulart, D. B. *Principles of Lactose Crystallization and Rheology of Milk Protein Concentrate*. Research, Society and Development, v. 10, n. 15, pp. 1-21. (2021). http://dx.doi.org/10.33448/rsd-v10i15.23028.

ILO-WHO (International Labor Organization-World Health Organization), *International Chemical Safety Cards (ISCSs) for Glucose*: https://www.ilo.org/dyn/icsc/showcard.display?p_card_id=0865&p_version=2&p_lang=en (2021).

Johnson, J.M and Conforti, F.D., *Lactose*: in B. Caballero, P.F. Finglas, and F. Tolda (editors) *Encyclopedia of Food Sciences and Nutrition* (Second Edition), Academic Press, pp. 3472-3476 (2003).

Motzer, W.E., *How Sweet It Is – Part 2* The VORTEX, v. 85, issue 4, pp. 6-8 (2023). www.calacs.org.

Sigma Aldrich, *Glucose Product Information*, https://www.sigmaaldrich.com/deepweb/assets/sigmaaldrich/product/documents/190/638/g8270pis.pdf (2022).

Williams, C.A., *Galactose*, in B. Caballero, P.F. Finglas, and F. Tolda (editors) *Encyclopedia of Food Sciences and Nutrition* (Second Edition), Academic Press, https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/galactose (2003).

USP Gray Zone Particulates Presentation is Available for Free

Donald MacLean

Subvisible and visible particulates testing for parenteral drug products (route other than digestive tract, inhalation, or topical) is less known and emphasized when compared to testing for concentration, identification, and active pharmaceutical ingredient (API) characterization. Part of the reason is Management support for testing fluctuates depending on what initiatives are hot, such as the 2009 FDA protein aggregation initiative for extended subvisible particles characterization, and the 2015 glass delamination issue. Another reason is some products are exempt from visible particulate testing requirement due to their use and physical appearance. The pharmaceutical compendia have two size ranges to consider, subvisible (1 micron to approx. 150 microns) and visible particles.

After initial 100% inspection, a portion of the product that passed inspection goes through secondary inspection where a statistical approach is used to accept or reject the lot. The term gray zone as used by USP (United States Pharmacopeia) presentation is a 30 to 70% probability that a visible particle size is detected. The acceptance zone is when there is less than a 30% probability of visual detection, which covers the subvisible particle size range. The reject zone is when there is greater than 70% probability of visually detecting a particulate. The gray zone covers the upper subvisible particulate size range and the lower visible particulate sizes. Figure 1 shows the POD versus particle diameter relation to the 3 zones. This assumes that the product is not meant to have particles.

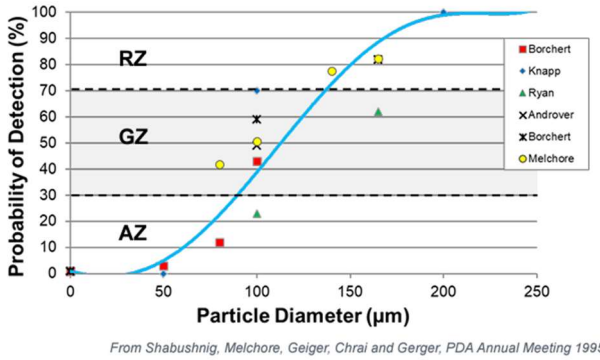


Figure 1. Probability of Detection versus Size.

Subvisible particles are detected through instrumental means such as light obscuration or filter microscopic means. USP <788> Particulate Matter in Injections (and Ph Eur 2.9.20) have 2 size limits, 10 and 25 microns with concentration limits based on container size and detection method. For ophthalmic products USP <789> Particulate Matter in Ophthalmic Solutions, 10, 25, and 50 microns based on detection method, which currently has the same concentration limits. See References listed at end.

Visible particles (greater than approx. 50 microns) are detected by machine or manually, but informational chapters focus on manual inspection. The ability to detect particles is affected by size, color, shape, refractive index, and most importantly by Operator. The three major pharmaceutical compendia have applied a statistical approach to particulates based upon lot size and levels (100% initial inspection uses General Inspection Level II). “Essentially free” is defined with an AQL (Acceptable Quality Limits) of 0.65% permits a small number of particles to be present. Visual inspection involves more than particulates and scores defects by severity (container integrity, particles, cosmetic). There

is no sizing for visual particulates. An interesting observation is that size is a good predictor of detectability, but it does not provide a good measure of clinical risk to patients.

– No size threshold above which particles always cause injury and below which they are safe.

– No controlled clinical studies to assess visible particle risk to patients. Only animal studies and anecdotal reports in humans. This is further complicated by how the product is used.

– Very large particles >500 µm will not pass through most needle canula but would be easily detected by visual inspection. Route of administration, number of particles, and patient population are important considerations when assessing particle risk.

USP (United States Pharmacopeia) has a free On-Demand recorded presentation from March 23, 2023 "All the Particulars on Particles: Gray Zone Particles" that is potentially important for cell and gene therapy.[1] The 4 speakers are either on the USP Dosage Forms Expert Committee, or USP Expert Panel on Visual Inspection of Parenterals. If you are interested in this topic go to

https://www.usp.org/events-training/course/all-particulars-particles-gray-zone-particles-demand

Here are **Key Points:**

- Particle characteristics (size-color-shape-density) will affect the probability of detection (POD); thus, not all particles will be detected with 100% probability.
- Product and package characteristics will also affect PoD.
- Gray Zone particles may be missed during 100% inspection yet may be seen during AQL (Acceptable Quality Limits) inspection, on stability, in retains, or even by the customer.
- Threshold studies are necessary to characterize inspection process performance.
- Subvisible test (USP <788>) data is useful when investigating gray zone particles found during visual inspection.
- Supplemental test methods are required when assessing compliance of difficult to inspect products (DIP) for visible particles.

Out of Scope and Future:

Note several areas are not bound by the USP <788>, <789>, <790> general chapters. These currently include gene and cell therapy (CGT). A webinar is planned for CGT in Q4 2023. USP has available chapters on visible inspection methods: USP <1790> Visible Inspection of Injections.

References:

1. https://www.usp.org/events-training/course/all-particulars-particles-gray-zone-particles-demand

2. USP <788> Particulate Matter in Injections
3. USP <790> Visible Particulate Matter in Injections
4. USP <789> Particulate Matter in Ophthalmic Solutions
5. USP <1790> Visible Inspection of Injections
6. Ph Eur 2.9.19. Particulate Contamination: Sub-visible Particles
7. Ph Eur 2.9.40 Particulate Contamination: Visible Particles
8. Ph Eur 2.9.53. Particulate Contamination: Sub-visible Particles in Non-injectable Liquid Preparations
9. Ph Eur 5.17.2. Recommendations on Testing of Particulate Contamination: Visible Particles
10. Ph Eur 11.2 Dosage Forms: Eye Preparations, text number 1163

Recommend Activity – California Bloom and Waterfalls

Donald MacLean

Figure 1. Peas planted between rows with other flowers. Glen Ellen in March.

After a few years of subnormal rain, this year's copious steady rain has caused an abundance of spring flowers. This month's recommended science activity is seeking spring flowers. Numerous locations abound. The best places are pastures near water, and hilly areas. That said uneven ground and streams create a treacherous hike, as we experienced last week when an elderly person slipped going across a stream and hit his head on a rock. There are various up to date references that can show where to go and what has been spotted.[1] I prefer the countryside as there are more fauna to see such as butterflies, snakes, and birds.

It is too late to view this year, but in February Fresno County Blossom Trail southeast of Fresno contains cherry, plum, peach, and apricot flowers that is impressive. The east side towards Sequoia National Park has a lot of oranges. The way housing is being constructed, the loop will be gone in 20 years.[2] An interesting observation is the citrus netting used for preventing seeds. Citrus is self-pollenating so bees are not necessary. The netting prevents cross pollination, therefore the citrus becomes seedless and more valued. Upon further inspection I noted a heavily coated blue substance on leaves that appears to be copper based used for fungus control.

Some of the flowers are like weeds, some are obviously planted. In the summer a marigold may be planted at the end of a grape row to act as a natural pesticide.

If hiking is too challenging, try a botanical garden.

Figure 2. Gartner snake on a trail in Sebastopol (Laguna de Santa Rosa).

One side effect from all this rain is temporary waterfalls. Mount Tamalpais is a good place to go. Cascade Falls in Mill Valley is within an urban environment with an easy stroll to see it. Dawn Falls west of Larkspur is a nice stroll but a bit of a climb. Cataract Falls southwest of Fairfax is a bit of a drive (watch out how you park) but easy to walk to.

Figure 3. Grass Going to Seed in Corte Madera in April.

Figure 4. Some locations have information signs such as this one in Fresno.

Figure 5. Flower at a botanical garden in Berkeley.

References:

1. https://www.sfchronicle.com/projects/2023/superbloom-map/
2. Fresno County Blossom Trail, https://www.goblossomtrail.com/