Edition 33

KARNATAKA REGISTERED PHARMACISTS ASSOCIATION

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MERRY

Christmas

HAPPY NEW YEAR

THE DRUG OBSOLESCENCE CHALLENGE

The pharmaceutical sector is a dynamic and adaptive one. Pharma professionals need to be clued onto changes with respect to marketing status of drugs. A situation that occurs with some drugs is obsolescence factor. Obsolescence is the process by which a drug becomes outdated and is no longer used. Obsolescence may happen due to new data on the side effects of a drug or availability of superior and safer new alternatives. For instance, cimetidine the first H_2 receptor blocker was a sensational entry into the market. However, side effects of cimetidine like gynaecomastia (breast enlargement in men taking cimetidine) and dizziness – contributed to the obsolescence factor of cimetidine; when a superior alternative H_2 receptor antagonist ranitidine entered the market – cimetidine was sent to the grave. History repeats! Ranitidine from 2020 seems to be on its last legs due to findings of impurity and suspected carcinogen NDMA (N-nitrosodimethylamine) in ranitidine formulations. Famotidine is the new star H_2 receptor blocker for heartburn, GERD (gastro-oesophageal reflux disease) and acid peptic disorder treatment. Manufacturers of ranitidine – Rantac (J B Chemicals), Aciloc (Cadila Pharmaceuticals), Zantac or Zinetac (GSK) - are all in a bind since demand for ranitidine tablets/suspension is contracting.

The Vioxx story

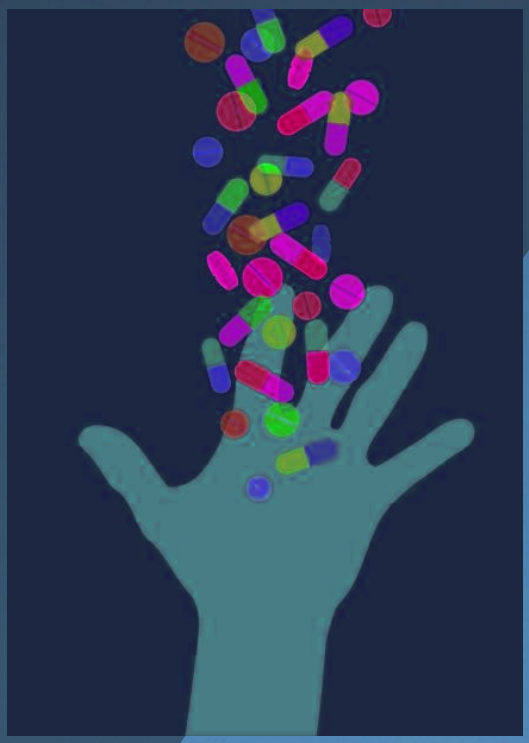
Another obsolescence story is that of rofecoxib (Vioxx from Merck) - a revolutionary specific Cox-2 inhibitor NSAID, which met its Waterloo in September 2004. Merck had launched rofexocib Vioxx with necessary marketing fanfare. In fact, Merck had asked US FDA to approve rofecoxib Vioxx, in Nov 1998, after conducting eight clinical studies involving 5400 patients. In Jan 1999, VIGOR study involving 8000 participants (half taking rofecoxib and another half on naproxen) was announced. VIGOR stood for Vioxx Gastrointestinal Outcomes Research Study, after all, specific cox-2 inhibitors were purported to have markedly lesser gastrointestinal side effects.

The VIGOR data and safety monitoring board appreciated that gastrointestinal side effects were lesser, but the incidences of stroke and heart attack in participants alarmed them. This happened in Nov 1999. VIGOR study results were controversial since the data was not properly presented in various journals including NEJM. The cardiovascular risks of Vioxx were not made clearly evident in the publications related to VIGOR study. After a lot of data crunching by seasoned researchers and discussions, and many court cases of affected patients, Merck in Nov 2007 announced the largest drug settlement amount in history, to litigants – Merck paid 4.85 billion USD (Approx., Rs. 36,723 crores). Merck had already pulled out Vioxx from the market in Sep. 2004

If the analysis of VIGOR study created obsolescence for rofecoxib (Vioxx, Merck), then in case of ranitidine it is a little known online pharmacy in Connecticut, USA called Valisure that is seemingly creating obsolescence for ranitidine. Today, Valisure does not have a pharmacy; it is focusing on independent drug testing only - as a lab. The pharmacy owned by Valisure closed down in 2021.

So what did Valisure do to put ranitidine on a probable pathway to obsolescence?

Before founding Valisure – the co-founder, Clark Joseph used to take generic medicines for his health problem, but continued to feel sick. He tested the medicine and was shocked to see the generic medicine was not of quality. When he escalated this problem to his pharmacist, the pharmacist brushed it off saying it must have been a problem batch. This stimulated Clark and his colleagues to start Valisure, the online and tiny brick-mortar pharmacy that tests medicines in its lab - before shipping to patients. It was during one of these testing practices (because Clark's daughter was taking ranitidine syrup) that Valisure discovered enormous abnormal amounts of NDMA (N-nitrosodimethylamine) in ranitidine tablets/syrup. Valisure detected 3 million nanograms of NDMA per tablet of ranitidine (due to higher temperature used in their testing procedure). US FDA states the safe limit of NDMA for human consumption is 96 nanograms per day. NDMA is a compound of nitrosamine chemical class, and above 96 ng/day consumption, NDMA is a probable (unproven) human carcinogen and is observed to be a carcinogen in animal studies. NDMA is described as a genotoxic material. NDMA is found in nature, plants and food too – in very tiny amounts, NDMA is not a problem. NDMA is a problem only in larger quantity - if more than 96 ng/day is consumed.



Valisure escalated the ranitidine NDMA problem to US FDA in June 2019. Thereby, in 2019 after investigation, US FDA also found NDMA (N-nitrosodimethylamine) in ranitidine tablets however it was in much lower levels - much less than Valisure's report.

How does NDMA get into the ranitidine tablet or syrup and then the body?

The most common route of NDMA (N-nitrosodimethylamine) contamination in ranitidine tablets/suspension is through improperly manufactured API (active pharmaceutical ingredient) - ranitidine. The solvent(s) used in API manufacture is the well-known source of impurities like NDMA. However, it is observed that long term storage of ranitidine tablets at higher temperatures (example: ranitidine tablets stored at 40 degree Celsius for more than 8 weeks) causes formation of NDMA inside the tablet through chemical reactions. And this may lead to more than 96 ng/day consumption of NDMA by an individual. Valisure also contends through its research that NDMA is generated inside the body when ingested ranitidine reacts with gastric acid contents and other body enzymes. However, official US FDA acceptance of this researched viewpoint is absent.

Similarly, Valisure in the past has shown that certain extended release tablets did not behave as claimed and they even proved that rapid release Tylenol (paracetamol) was dissolving slower than regular paracetamol!

Overall, there is no firm clarity that NDMA is a human carcinogen (although in animal studies, NDMA is understood to be a carcinogen). And there are contradictory points of view on the potential of ranitidine tablet/suspension to have high level of NDMA impurity.

Ranitidine status in USA and UK

In UK, ranitidine was removed from pharmacies in Oct. 2019 and US FDA has ensured ranitidine is unavailable in USA from April 2020. EMA (European Medicines Agency) does not permit marketing of ranitidine. In India, ranitidine is off the NLEM 2022 list, but marketing is allowed. Once there is a clear picture on ranitidine marketing status internationally including WHO opinion, Indian regulatory agencies will likely take appropriate action.

Lawsuits

In USA, lawsuits are being filed by ranitidine users. The lawyers quote a Taiwanese study that ranitidine increases incidence of gastric, liver and other cancers – in their bid to extract damages or settlement.

Past glory of Zantac

Zantac (GSK) has enjoyed crowning glory in the market – launched in early 1980s Zantac went onto becoming a blockbuster brand (1 billion USD global sales in 1988). In 1990, the global sales of Zantac was 2.40 billion USD. In fact, in 1990, Zantac was 50% of GSK's total annual sales. In India and abroad, ranitidine has been one of the most prescribed drugs in terms of units. Today, it is a story of obsolescence and fading glory. The Vemegal, Karnataka manufacturing facility owned by GSK was sold off to Hetero Drugs due to slump in demand for ranitidine tablets and financial stress. GSK is trying to come back to old glory with a new launch - Zantac 360 in USA – the drug is famotidine H_2 receptor blocker.

J B Chemicals (manufacturer of Rantac brand of ranitidine), in India, have launched RANRAFT – an antacid liquid with sodium alginate acting as a raft with the antacids on the raft - to neutralize excess HCl acid in stomach. This is to help protect its business of heartburn management.

Obsolescence is a part of the drug life cycle as newer data points emerge from clinical studies. And newer safer drugs are a trigger for obsolescence of older drugs. The ranitidine 'obsolescence story' is causing heartburn to some stakeholders. However, we pharmacists and pharma professionals need to adapt to the obsolescence phenomenon, and constantly update ourselves on the marketing status of medicines.

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NEW BORN SCREENING FOR HYPERBILURUBINEMIA

Hyperbilirubinemia is a medical condition in which babies have very high levels of bilirubin in their blood. When the body breaks down blood cells, it makes bilirubin. Babies with hyperbilirubinemia have trouble getting rid of this chemical, causing it to build up in the blood and body. When high levels build up, it can damage the brain cells. Without treatment, severe hyper-bilirubinemia may lead to permanent brain damage.

Bilirubin screening is a common practice to screen every newborn for high bilirubin levels in the blood (hyperbilirubinemia). The screening is performed before the baby discharged from the hospital. It needs taking a small sample of blood from the baby's heel. This is then tested in a laboratory. High levels of bilirubin can cause jaundice. This is a common condition in the first few days of life, and it normally cured by itself. But if bilirubin levels are very high, the baby may need treatment to prevent serious problems, such as brain damage. Screening can detect high bilirubin early and help to get the right treatment for the baby. For this reason, most parents follow expert medical advice and allow this screening.

Most screening results come back normal, and parents don't need to follow up. But if the baby's results show that baby is at risk, it is recommended to repeat the test a day or two after the baby goes home. It's very important that to have the follow-up to be done. This is the only way to make sure that the baby is safe from the serious effects of high bilirubin.

How are newborns screened for hyper-bilirubinemia?

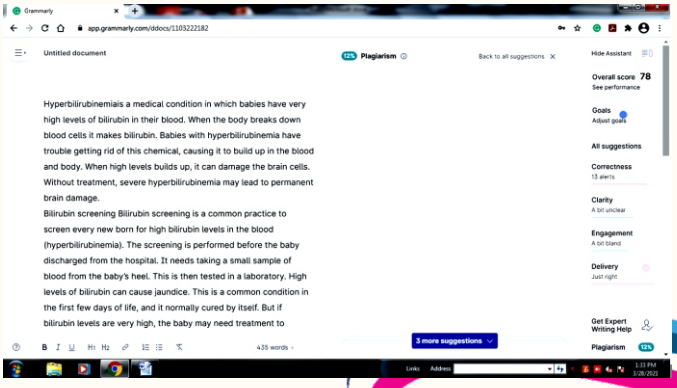
Newborn screening for hyperbilirubinemia can be done during the first days of life at the bedside in the hospital. It is not the part of routine, blood spot-based screening. However, some of the blood taken for the routine screening can also be used to screen for hyperbilirubinemia. To screen for this condition, nurses and doctors can check newborns for yellow eyes or yellow skin. This process of visual check can be inaccurate and does not measure exact bilirubin levels. In order to measure accurate bilirubin levels, health care persons often use a painless skin sensor.

How is hyperbilirubinemia treated?

Two treatments can prevent or even reverse some NH symptoms.

Light therapy - This therapy is also known as “phototherapy.” It involves shining special blue lights on babies with hyperbilirubinemia. The lights help the body break down extra bilirubin. This lowers bilirubin levels and reduces the risk of symptoms of hyperbilirubinemia.

Exchange transfusion - This sort of therapy involves changing some of a baby's blood with blood from a healthy donor. It helps in reducing the bilirubin levels and reduces the risk of symptoms of hyperbilirubinemia. Only babies with very severe hyperbilirubinemia need this treatmen



New Born Screening for Heart Defects

Congenital heart disease (CHD) is a problem in the structure of the heart or the blood flow through the heart. If the CHD is serious, called a critical congenital heart defect (CCHD), it is required to detect and repair early in a baby's life to prevent other health problems. Congenital heart disease (CHD) is the most common congenital disorder in newborns. Critical CHD, defined as requiring surgery or catheter-based intervention in the first year of life. Although many newborns with critical CHD are symptomatic and identified rapidly after birth, others are not diagnosed until after discharge from the birth hospitalization. In infants with critical cardiac lesions, the risk of morbidity and mortality increases when there is an interruption in diagnosis.

Consequences of Late Detection

Most of the newborns with critical CHD are diagnosed either prenatally or upon clinical examination during the birth in the hospital. However, in few infants with critical CHD appear normal on routine examination, and signs of critical CHD may not be apparent in the first days of life. Cyanosis may not be clinically apparent in patients with mild desaturation or anaemia. In darkly pigmented infants, cyanosis can be especially difficult to appreciate.

Benefits of Screening

Early detection of critical CHD – The primary benefit of newborn screening for critical CHD with pulse oximetry is timely detection of infants with critical CHD prior to discharge from the birth hospitalization, thereby reducing the morbidity and mortality associated with delayed diagnosis.

Criteria for positive screen — Criteria for a positive screen using the American Academy of Pediatrics (AAP) algorithm) include any of the following:

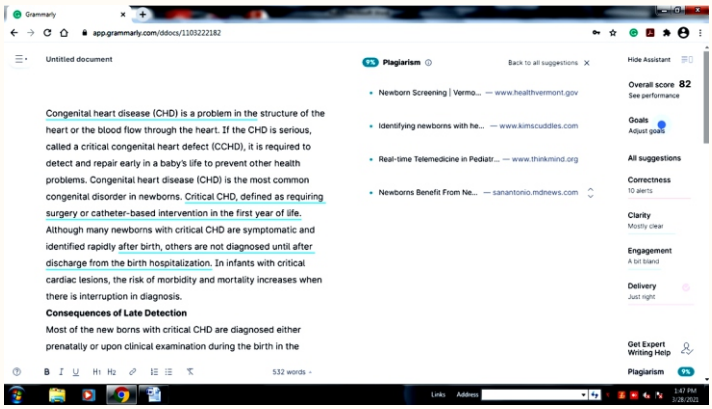
- Oxygen saturation (SpO2) measurement <90 per cent in either extremity
- SpO2 measurement 90 to 94 per cent in both upper and lower extremities on three measurements, each separated by one hour
- · SpO2 difference >3 per cent between the upper and lower extremities on three measurements, each separated by one hour

Criteria for negative screen:

Infants with negative screening results who are performed clinically well without signs concerning possible CHD do not require additional evaluation. However, it is important to identify that infants with a negative screen may still have critical CHD because hypoxemia may not be present all of the time in some CHD lesions. It is assessed that universal newborn screening with pulse oximetry may omit as many cases of critical CHD as it detects. Screening with pulse oximetry cannot void the presence of a critical CHD. If there is clinical suspicion for critical CHD, additional evaluation should be performed even in the setting of a normal pulse oximetry result.

Pulse oximetry is a non-invasive test that detects how much oxygen is in the blood. Infants with heart problems may have low blood oxygen levels, and therefore, the test can identify babies that may have Critical Congenital Heart Disease (CCHD). The test is done using a painless sensor placed on the baby's skin. If screening with pulse ox identifies a baby with low oxygen, the care team will probably order additional testing.

The goal of CHD screening in newborns is to decrease the mortality and morbidity related to delayed diagnosis by recognizing infants with critical CHD in a time to time manner. There is evidence that universal screening with pulse oximetry progresses the identification of patients with critical CHD related with physical examination alone and may lead to decreased infant mortality from critical CHD.



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ADICHUNCHANAGIRI UNIVERSITY

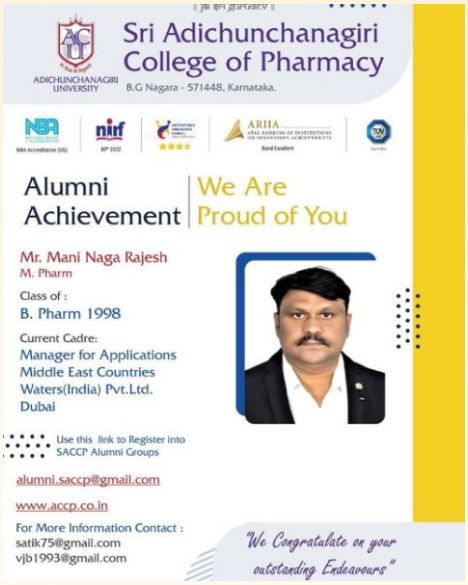
Sri Adichunchanagiri College of Pharmacy

CAMPUS BUZZ!

Sri Adichunchanagiri College of Pharmacy.
Zilla Panchayat,Youth Empowerment and sports, and Neharu Yuva Kendra Mandya.
Organised district level Youth Festival on 24-11-2022 at Mandya.
Four students from our college participated in the Pick and Speech competition and ***Mr Arif Allabakhash Turubkhan*** from B.Pharm Sem V,
won FIRST PLACE and he is now selected for state level.

Alumni Achievements.

Nov 2022



Adichunchanagiri Center for Entrepreneurs, students from Sri Adichunchanagiri College Of Pharmacy attended the "Global Investors Meet 2022"

at Bangalore on 2nd November 2022.

Prime minister Sri Narendra Modi inaugurated the event and addressed a large gathering of lawmakers, industry leaders, technocrats and entrepreneurs.

"We've freed our investors from red-tapism and given them a red carpet of opportunities. Instead of making new complicated laws, we rationalised them,"

Three Union ministers -- Finance Minister

Smt Nirmala Sitharaman, Industries Minister Sri Piyush Goyal, and Coal and Mines Minister Sri Pralhad Joshi -- along with Chief Minister Sri Basavaraj Bommai and state cabinet ministers were present during the event and addressed the gathering.

The students received various insights on the global economy and investors perspective, the majority of the investment was to develop Karnataka and India and nurture the startup ecosystem which counted for a overall sum of around &5 lakh crores.

CAMPUS BUZZ!

Al-Ameen College of Pharmacy, Bangalore

The Institution Innovation Council (IIC) of Al-Ameen College of Pharmacy, Bangalore conducted a Motivational Talk under the theme: "My Story-Motivational talk of a Successful Innovator/ Entrepreneur" on 28th Nov-2022

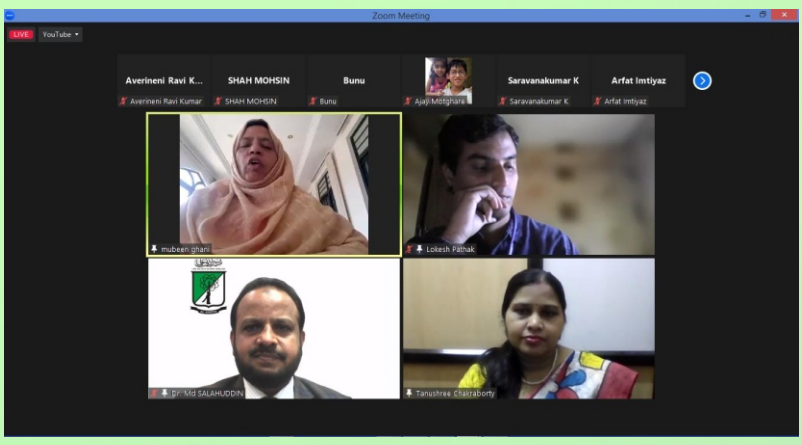
The Eminent Speaker was Mr. SHAMEEK CHAKRAVARTY, Co-Founder & CEO, Farmizen, Bengaluru". He spoke on the theme highlighting his journey from an IITian to StartUP Founder & Innovator. He gave insight on his Branding of Farmizen through organic farming.

We are very much Greatful to Mr. Shameek Chakravarty for accepting our invite and delivering a informative Motivational talk.

The Institution Innovation Council (IIC) of Al-Ameen College of Pharmacy, Bangalore conducted a Motivational Talk under the theme: "My Story-Motivational talk of a Successful StartUP founder" on 26th Nov-2022

The Eminent Speaker was Dr. LOKESH PATHAK, Co-founder & Head, Global Procurement, MCLOB USA LLC". He spoke on the theme highlighting his journey from a Pharmacist to a StartUP founder.

We are very much Greatful to Dr. Lokesh Pathak for accepting our invite and delivering a informative Motivational talk.



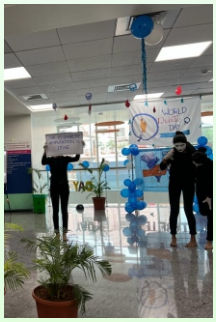
CAMPUS BUZZ!

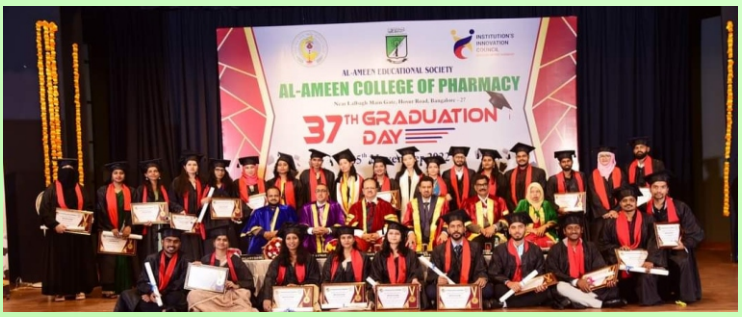
Al-Ameen College of Pharmacy, Bangalore

Department of Pharmacy Practice, NSS Unit & Institution Innovation Council (IIC) of Al-Ameen College of Pharmacy, Bangalore in Association with St. Philomena's Hospital, Bengaluru observed 'WORLD DIABETES DAY' with the theme "Access to diabetes care" on 14th Nov-2022.

On this occasion our Pharm-D students performed skit to educate the patients on Diabetes, measured Random Blood Sugar Level of about 50 people and monitored BP. Distributed Pamphlets & displayed an educational video on diabetes in the OPD.

The day has its significance to reach the maximum number of people globally to promote a platform to cure diabetes and its treatment. And in the year 2007, a blue circle logo was initiated by the UN as a global symbol to create awareness regarding the disease diabetes and the community associated with it.





Awards for BEST OUTGOING STUDENTS

Bank of Baroda has choosen Al-Ameen College of Pharmacy, Bangalore for presentation of BoB Achievers Awards to students. The awards were presented to 3 BEST students of AACP of B.Pharm, Pharm-D & M.Pharm during the 37th Graduation Day. Regional Manager of BoB, Mr. Praveen Kumar Singh along with Mr. Ramakrishna Kalluri Bank Manager presented Rs. 31,000/- each to Ms. Manasa N (M.Pharm), Ms. Shruti (Pharm-D) & Ms. Priyanka Naik (B.Pharm) as BoB Achievers award.

Ms. Kanishree (B.Pharm) received 'SS Award' of Rs. 10,500/- as Best Outgoing student Instituted by Former AACP employees Dr. Shyamala Bhaskaran & Dr. Sarsija Suresh.


CAMPUS SNIPPETS

Al-Ameen Pharmacy College Marks 37th Graduation Day

Al-Ameen College of Pharmacy, Bengaluru, celebrated its 37th Graduation Day on November 5. The Chairman Al-Ameen Educational Society, Umar Ismail Khan in his presidential address highlighted the efforts of the Secretary Zubair Anwar and Principal Dr. Md. Salahuddin.

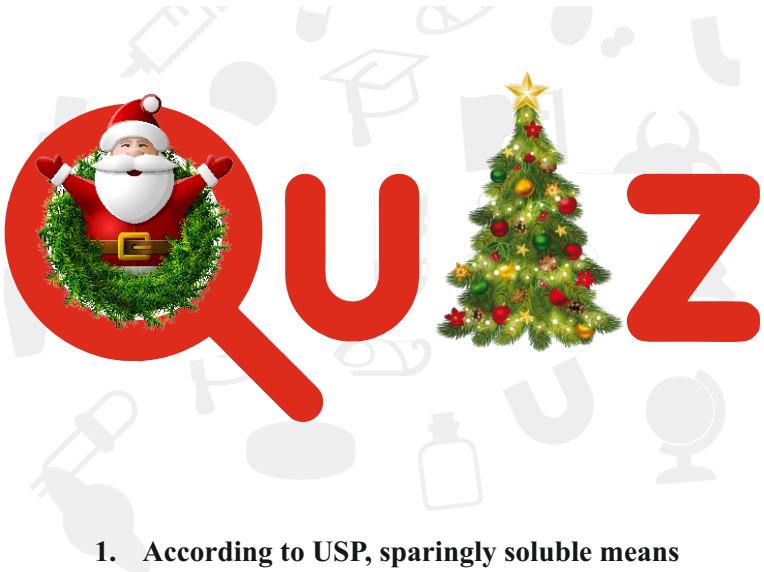
Chief Guest, Dr. S. Sacchidanand, former Vice-Chancellor of Rajiv Gandhi University of Health Sciences, Bangalore in his address appreciated the successful 40-year Journey of Al-Ameen College of Pharmacy. He said, "Graduates are lucky to be called alumni of Al-Ameen and its certificates have a lot of goodwill globally". He emphasised on social responsibility of students and asked them to contribute to the society. He emphasised undergraduate students to take up higher studies. He spoke on the values of Research Institutes and how Al-Ameen is contributing to education in the light of NEP.

Graduation certificates were conferred upon 117 students of B.Pharm, M.Pharm, Pharm-D and Pharm-D (PB). The Graduation Certificates were handed over by Chief Guest and also the Guest of Honour Mr. Zubair Anwar.

Chief Guest Dr. Amaresh Tumbagi, Deputy Drugs Controller said, "Indian Pharmacists have reached to global level and valued more due to immense contribution during covid times. He said that more than 40% of the Biotechnology Industry and 65 ADR centres are in Karnataka. He emphasised on commercialisation of research work carried out at institute level with the support of Government. He updated students on the scope of Pharmacy, Drug discovery, research, academics and in industry.

The students – Priyanka S. Naik (B.Pharm), Sruthi (Pharm-D) and Manasa N. (M.Pharm) received Bank of Baroda Achievers award each of Rs. 31,000 as outstanding outgoing students.

Three books authored by Ayesha Syed, Dr. Salahuddin for Pharm-D students were released on the occasion. Dr. Mubeen Ghani, Vice-Principal proposed the vote of thanks.



RULES

1. Correct answers will be rewarded 2 point each (20 marks)
2. Answer of the quiz will be evaluated by panel of judges and their decision is final. (Max mark:20)
3. Those who get the highest marks, their photo will be published in our next bulletin and also a cash prize of Rs.500/- will be rewarded to them
4. The answer must be sent within 25th Dec. 2022 to this E Mail ID- krpaindia@gmail.com
5. A confirmation mail will be sent to you on receiving your e-mail.

1. According to USP, sparingly soluble means the parts of solvent required for one part of solute is …….?

a. 10-30
b. 30-100
c. 100-1000
d. More than 1000

2. How much concentration of Benzalkonium chloride is used as preservative in eye drop?

a. 1.00% w/v
b. 0.10% w/v
c. 0.01% w/v
d. 0.05% w/v

3. For Maize starch preparation, the temperature should be ……..?

a. More than 50°C
b. More than 60°C
c. More than 70°C
d. More than 90°C

4. International Organization for Standard-ization, ISO class 8 is equivalent to ?

a. Grade-A
b. Grade-B
c. Grade-C
d. Grade-D

5. Which BCS class shows High Solubility and Low Permeability ……?

a. BCS Class I
b. BCS Class II
c. BCS Class III
d. BCS Class IV

6. A drug substance is considered highly soluble when the highest strength is soluble in ……?

a. 200 ml
b. 250 ml
c. 300 ml
d. 500 ml

7. If Log P value is more, the compound is …….?

a. Hydrophilic
b. Hydrophobic
c. Neutral
d. None of the above

8. **Wetting agent has ……. HLB (Hydrophilic–lipophilic balance) value.**

a. 1 to 3
b. 3 to 6
c. 7 to 9
d. 8 to 18

9. Pharmacovigilance is a part of …….

a. ICH E1 guidelines
b. ICH E3 guidelines
c. ICH E2 guidelines
d. ICH E2 (A-F) guidelines

10. pH of the solution is calculated by ……?

a. Henry's law
b. Charles law
c. Dalton's law
d. Henderson-Hasselbalch equation

Congratulations

to the winner of Thirty Second Edition

KRPA Quiz Competition

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Remember
What is not defined, cannot be improved
What is not improved, cannot be measured
And, finally
What is not measured, cannot be achieved
- Define, Improve, Measure and Achieve
Good luck and my best wishes to you all

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Train Your Brain to Frame Your Mind

Key formulas to activate your inner super power as to achieve the peak performance
In colloquial terms, the words mind and brain may be used interchangeably but, the two are in fact not the same. Brain is a physical organ, while mind is an functional. When compared to a computer, the brain acts as the hardware while the mind is the software within it. As you can upgrade your computer system by adding newer software or features similarly one can reprogram the mind for success and self transformation
Transformation happens in action, not in thinking and gaining knowledge in itself. It's about going beyond that and doing something that can bring results.
Challenge is most of us think that we are great just based on the limited knowledge that we have. We may have it, but the importance is what have we done with that knowledge. Much before that how convincing, clear and clarity that we have.
How much are we aware at conscious level and how much our subconscious support to use it.
Have I built skills to utilize/ demonstrate the knowledge is a question that needs to be pondered????
5 reasons why most people never reach their true potential.

- They keep on adding newer learning but fail to use something which is already learnt
- They get influenced easily by people and start acting upon without realizing their potential and uniqueness
- When they lose, start overthinking and finally quit but fail to put persistent efforts
- They get instant external motivation and take action without understanding the process, rules, concepts, strategies, planning, do's and don'ts...etc.
- They sit with problem centric mindset, will start giving reasons

So what's the solution?
Following three decisions are important to happen in the mind

- Your decisions about what to focus on.
- Your decisions about what things mean to you.
- Your decisions about what to do to create the results you desire.

It is your decision and not your conditions, that determine your destiny. - Tonny Robbins

Morris Goodman-The Miracle Man talks on the power of mind and visualization
He says "Once you have your mind, you can put things back together again".
He continued to add "I could not have afford to allow anything to come in my mind that will distract me from my goal and from my vision"
Man becomes what he thinks about
So, the ultimate further step is You just need to take proper action at the right times to get massive results!
Simply select the areas that you want to improve in like mood, focus, productivity & Ultimate Self Development mindset will build your powerful routine to improve in those areas & reach your goals!

Motivation is about Inside Out, Not from Outside In.
The Neurons in your brain that are fired together will wire together to create neural pathways. Which means continual repetition of self talk/ incantations are the key tool for achieving the desired
So it requires a conscious awareness and an ability to align all our senses in one direction to attain and accomplish the desired.
Whenever change happens, happens within a moment. That's the time the change begins.
Whenever something changes in life, following things need to happen in our brain and reality .

1. First of all, we need the clear-cut idea about what exactly is to be changed. If we don't know what is to be changed, then change won't take place. Which means being aware of What do you really want to change in your life? Do you have a clear & exact idea of what is to be changed or improved in your life? That clarity is important.
2. Model of operation should be at necessity to change. That conviction is important. This has to be changed in any condition' is necessary.

Half-hearted efforts can't change anything. Water evaporates only at 100° Celsius. Change happens only when we reach that point from where there is no other way except changing ourselves. When we feel in our heart, 'Now, enough is enough,' the change occurs.
Have you reached/ generated that point, where you are feeling 'this has to be changed at any cost'?

3. Doer or person who looks for change would have had attitude that whatever is to be changed, he would take responsibility for it. People don't change because every time they throw the responsibility on others' shoulders. They always give reasons for not changing. That's why don't give logic, take responsibility for yourself. Have you taken 100% responsibility for yourself?
4. There should be trust as: I can do, I can be, I can change, I can create. It should be very clear in our brain that I can change the situation. Do you have faith in 'I can change' attitude?
5. There has to be strong purpose for change, benefits needs to be felt, imagined. Visualizing as if change has brought in the desired outcome.
6. Take actions, build required capabilities, keeping your behaviour flexibility
7. Operate yourself from physiology and psychology of excellence
8. Believing the results, process of achieving, keeping persistent efforts.

Performance enhancement is about breaking complex problems in to simplex, because mind understands simple and specific things. In order to drive ourselves, we need to make internal specific positive dialogue to establish the productive state of mind.