

Science Last Fortnight

Low and High Vitamin Doses

In cancer treatment

Colorectal cancer is the third most common cancer. It is thought to be caused by mutations in the *KRAS* and *BRAF* genes. While dietary fibre plays a role in preventing colorectal cancers, dosage remains an issue with water soluble vitamins – Vitamin B3 and Vitamin C. These vitamins appear to have some therapeutic action on colon cancer.

Bipasha Bose, Utsav Sen and Sudheer Shenoy from the Yenepoya University, Mangalore now report that low doses of Vitamin B3 and Vitamin C promote proliferation of colon stem cells while very high doses result in apoptosis, programmed cell death of cancer stem cells.

The researchers used HT-29 and HCT-15 colon cancer cell lines for their experiments. They put small concentrations (5–25 μM) of Niacin and Vitamin C in a culture medium and, using analytical flow cytometry, found that the number of cancer stem cells increased. But when higher concentrations (100–1000 μM) were used, the cancer stem cells were reduced. The scientists used a MTT assay to assess percentage cell growth and, by differential staining of dead alive cells, established that a larger number of cancer cells died due to higher amounts of Vitamin C and Niacin in a dose-dependent manner. The high doses of the vitamins did not have any deleterious effects on other normal cells such as fibroblasts.

This differential expression of cancer stem cells towards different concentrations of the same vitamins is attributed to antioxidant defence mechanisms. High doses inhibit the cellular antioxidant defence machinery and are responsible for the reduced expression of catalase and superoxide dismutase – the key enzymes of cell growth. The reduced expression of the superoxide dismutase is one of the possible reasons for the death of cancer cells when exposed to high doses of vitamins. Increased doses of the vitamins may lead to reactive oxygen spe-

cies-mediated apoptosis, say the scientists.

The effect of the vitamins on cancer stem cells seems to be ambivalent. More research is needed to understand the mechanisms of these nonlinear effects of vitamin dosage given to cancer patients. Meanwhile, doctors need to consider the dosage of vitamins as a critical factor in curing colorectal cancers.

Cell Biol. Int., **41**(10): 1127–1145

Detecting Chikungunya Outbreaks

Fog-based cloud computing

Chikungunya is a rapidly spreading infectious virus transmitted by mosquitoes. A sudden onset of fever and severe joint pains are typical symptoms. Such threats to public health can reach epidemic proportions without adequate early detection. With the advances in mobile technology, it is getting easier to design cloud-based health services which can detect outbreaks early enough. However, latency issues pose a challenge in the transmission of data. And can lead to inaccurate diagnosis.

Last fortnight, Mahajan from GNDU, Punjab proposed introducing a fog layer – an intermediate layer between cloud and sensor layers – to address latency issues. This fog-based system provides a remote diagnosis based on user health symptoms and surrounding environmental conditions.

Data about health, environment and meteorology is collected using a wireless sensor hardware device. The data accumulated in a sensor layer is sent to the fog computing layer, which processes the data and categorizes the user as infected or uninfected. The user is then alerted based on severity.

Diagnostic and emergency alert messages generated from the fog layer are stored in the cloud layer. This layer also contains information about the location of mosquito dense and breeding sites. This data helps project the probability of the spread of the infection or vulnerability to it.

The team evaluated the performance of the system using symptom datasets

from consulting specialists. They report better bandwidth efficiency, minimum execution time, and minimum delay in generating real time notifications. Government health care agencies can now take measures to control outbreaks by implementing this new technology.

Comp. India, **91**: 33–44

Amoeba, Stop Moving!

Blebbing at the molecular level

Amoebic dysentery or amoebiasis is a major health problem in developing countries. The amoeba, *Entamoeba histolytica*, that causes this disease, is a human gut parasite. The motility of the parasite is important for the invasion and spreading of the infection in humans. It also helps amoeba escape the host immune system.

Blebs are small bulges of plasma membrane that help amoeba to migrate on resistive gut epithelial cell lining during infection. Blebbing is an essential process for the amoeba in the growing stage while absorbing nutrients from humans. Interestingly, a similar process is observed in the early developmental stages and in cancer metastasis in human. But, molecular mechanisms for blebbing are not yet understood.

Recently, Ravi Bharadwaj and other researchers from the Jawaharlal Nehru University studied the role of EhRho1 protein from *Entamoeba histolytica* in blebbing because it resembles the RhoA in humans. They carried out several experiments to decipher the role of amoebic EhRho1 and other molecules that regulate blebbing.

The team confirmed that parasitic EhRho1 signals through lipids in plasma membranes. Lysophosphatidic acid enhances blebbing by elevating the active EhRho1 level and phosphatidylinositol 4,5-bisphosphate reduces bleb formation. The researchers suggest that Rho1 regulates specific phosphoinositol 3 kinase pathways which modulate phosphatidylinositol 4,5-bisphosphate level in the plasma membrane, thereby controlling bleb formation and the motility of the parasite.

They concluded that blocking blebbing inhibits amoeba cell motility and consequently pathogenesis. They also propose that inhibiting EhRho1 and other molecules in Rho1 signalling pathways can provide a new therapy for amoebiasis. This is the first report on understanding the molecular mechanism of bleb formation in amoeba.

This study will be helpful in understanding related pathways in humans and for treating cancer in future. The researchers are, however, cautious about their discovery. It is not clear whether Rho1 initiates blebbing or whether there is another initiating factor that recruits Rho1.

Cell. Microbiol., **19**: e12751

Insulin Ameliorates Memory

Intranasal spray for Alzheimer's?

Alzheimer's is a slow progressive, devastating neurodegenerative disease that destroys memory. According to a WHO Alzheimer 2015 report, more than 45 million people live with this disease, and it is predicted to affect 131 million people by 2050. The chance of getting this disease increases with age and the risk doubles every five years. So far, experimental drugs have failed to make a significant difference in slowing the disease.

Last fortnight, researchers from the Central Drug Research Institute, Lucknow in collaboration with the Academy of Scientific and Innovative Research, Chennai developed a method to treat Alzheimer's disease: insulin. Insulin is secreted by the pancreas and reaches the brain to help convert blood sugar to energy. Reduced insulin level leads to energy deficiency in the brain that results in cell death and eventually causes memory loss. Reduced insulin supply to the brain may be one of the causes for this disease.

The researchers tested this possibility by administering insulin to the brain through intranasal delivery to chemical induced memory impaired rats. They found that intranasal administration of insulin ameliorated memory in the rats. Moreover, the insulin delivered through this route did not alter blood glucose levels, which indicates that the method does not pose

the risk of developing hypoglycaemia – low blood sugar.



Image courtesy: ABC news

Alzheimer's is a common brain degeneration disease in the elderly. That intranasal administration of insulin halted Alzheimer's in rats is encouraging. However, clinical trials are needed to evaluate its potential in the treatment of Alzheimer's in humans.

Mol. Neurobiol., **54**: 6507–6522

Advances in Drug Delivery

Use of hybrid-nanoparticles

Nanoparticles are often used to deliver drugs effectively, in a targeted manner, to specific sites because of their high penetrability. However, some of these small particles have severe side effects. So scientists are searching for biocompatible nano-molecule systems with reduced side effects.

Last fortnight, scientists from the Mahatma Gandhi University, Kottayam, synthesized self-assembled lipid-polymer hybrid nanoparticles for drug delivery to treat HIV-AIDS. Zidovudine is the first USFDA approved drug for the treatment of acquired immunodeficiency syndrome caused by the human immunodeficiency virus. They prepared zidovudine loaded hybrid nanoparticles of alginate and stearic acid–poly ethylene glycol using a double emulsion solvent evaporation method.

This hybrid system has a hydrophilic polymeric core and a shell embedded with a lipid–polyethylene glycol envelope. The drug is encapsulated within the hydrophilic core, and is stabilized by the lipid shell. This increases the drug loading capability and provides

protection against gastrointestinal fluids.

The researchers also found that the dendritic structure of the hybrid-nanoparticles efficiently holds zidovudine. 'In this drug delivery system the drug is released in a controlled and sustained manner to avoid excess drug accumulation in the nearby tissues that causes unwanted side effects' says the paper's lead author.

Int. J. Biol. Macromol., **103**, 1265–1275

Damaged Bone Architecture

Botanical repair

Age-related damage in bone architecture – osteoporosis – is a silent disease. It does not make its presence and progression felt. The disease is prevalent in postmenopausal women. Declining levels of estrogen disturb the balance between bone tissue regeneration and degeneration, resulting in reduced bone density and fragile osteo-architecture. Estrogen therapy does little to cure or prevent the disease and is not popular due to side effects. A team of scientists from the CSIR-Central Drug Research Institute, Lucknow have now come up with an encouraging solution for the management and cure of this problem.

Ritu Trivedi and colleagues evaluated the effect of an alcoholic extract of heartwood – the inner part of the trunk of the *Dalbergia sissoo* tree – on bone pathology. From a phytochemical investigation of the alcoholic extract of heartwood, they discovered four phytoestrogens – Dalbergin, Dalbergiphenol, Dalsissoal and Latinone – in the extract. The scientists hypothesized that these phytoestrogens might provide an estrogen-like effect and prevent osteoporosis.

The team focused on bone fragility and alteration in microarchitecture as parameters. They used ovariectomized rats to mimic postmenopausal conditions. And found that, after treatment with the alcoholic extract, the biomechanical strength and microarchitecture of the bones of these rats were at par with those of estrogen treated rats.

The scientists then hypothesized that the extract may be activating osteoblasts. If that is the case, the extract could be used for faster healing of

fractured bone. They used a drill-hole injury rat model to mimic bone fracture conditions. After treatment with the extract, the rats showed faster healing and bone tissue regeneration than could be observed in the control.

The alcoholic extract did not show any liver and uterine toxicity in the treated animals in both experiments.

These preclinical experiments by the CDRI scientists suggest that phytoestrogens from *Dalbergia sissoo* have potential in protective and curative treatments of bone conditions. Further work is needed to translate these results and develop a safe, potent, and economic therapy for postmenopausal osteoporosis and fragile bone fracture.

J. Pharm. Pharmacol., **69**(10): 1381–1397

DNA Chip Based Sensor

Identifying Streptococcus pyogenes

Affecting some 700 million people every year, *Streptococcus pyogenes* can cause mild skin or throat infections and can even lead to life-threatening toxic shock syndrome. If not treated early, it can result in rheumatic heart disease and heart valve damage. Conventional diagnostic techniques are time-consuming and labour intensive, requiring experienced professionals and sophisticated equipment. To properly address this menace, we need accurate, simple and affordable pathogen identification devices with rapid response.

Researchers from the CSIR-Institute of Genomics and Integrative Biology and the National Centre for Disease Control, New Delhi have recently developed a DNA chip-based sensor for the quick detection of *Streptococcus pyogenes* from patient throat swab samples. The DNA chip-based sensor consists of a carbon electrode embedded with gold nanoparticles. The working electrode surface of the sensor is attached to several small-sized, single-stranded DNA probes specific to the pathogen. The team validated the use of the chip with suspected real patient samples.

When DNA, isolated from patients' throat swabs, comes into contact with the surface of the sensor, it binds to the complementary single-stranded DNA on the device, leading to measurable

electrochemical change. This DNA chip is highly specific for *S. pyogenes*. It could identify the pathogen even at very low concentrations of DNA. The sensor could even detect 60–65 bacteria in a 6 microlitre sample.

The team found that the sensor is stable for 12 months with only 10% loss in an initial current peak on storage at 4°C.

Int. J. Biol. Macromol., **103**: 355–359

Handling Fabric Effluent

Bioremediation by bacterial granules

Textile industries are major contributors of effluent discharge. Fabric dyes are recalcitrant to degradation and lower dissolved oxygen levels, harming aquatic ecosystems. Eliminating these dyes from the environment is a major challenge. Since physico-chemical methods of purification consume energy or create other undesirable environmental effects, researchers are racing to find ways of bioremediation of wastewater using plants or microbes.

Last fortnight, researchers from the Pune University and the National Centre for Cell Science, Pune reported detoxifying reactive blue 4 – a phytotoxic, cytotoxic and genotoxic dye – using microbial granules.

They cultured the aerobic bacterial granules in a fermenter. And confirmed the community composition of these self-immobilized aggregates of microorganisms in the granules by sequencing and bioinformatics analysis. Using scanning electron microscope images, the scientists characterized the morphology of the granules.

The team then performed dye degradation studies at varying reactive blue 4 concentrations in the presence of bacterial granules. They checked the organic load of reactive blue 4 in terms of chemical and biological oxygen demand and total dissolved solids. The team observed dye degradation to be prominent under static conditions. They examined the effects of temperature and pH on the degradation to optimize the process.

The scientists claim that the bacterial granules metabolized products to nontoxic by-products. Bacterial granules have the capacity to withstand

high organic load and have good biomass retention capacity. Textile industries would do well to apply this economical and efficient method of bioremediation using aerobic bacterial granules.

Water Res., **122**: 603–613

Chakkota Fruit Juice

Nanoparticle production

Due to its acidic nature, vitamin-C rich Chakkota fruit juice, a popular beverage, has recently been used to produce nanoparticles which can work as antibacterials or as sensors to detect the concentration of dopamine, a neurotransmitter, in solutions.

Last fortnight, researchers from the Siddaganga Institute of Technology and the Tumakuru University produced zinc oxide nanoparticles from Chakkota fruit juice. These were then used for accelerating reactions, as antibacterials and as electrochemical sensors for the concentration of dopamine in solutions. To make the nanoparticles, the researchers mixed zinc nitrate with dilute Chakkota fruit juice and kept it at high temperature – 400°C – for 4–5 minutes to obtain zinc oxide nanoparticles. X-ray diffraction and electron microscopy show that these particles have hexagonal structure.

Then, the team tested these nanoparticles against three strains of bacteria – *E. coli*, *S. aureus* and *K. aerogenes*. And found them effective against the latter two.

The ZnO nanoparticles act as good catalysts for the degradation of methylene blue dye, an industrial effluent from textile and other industries. These particles were also used to make a ZnO modified glassy carbon electrode which turned out to be a sensitive detector of dopamine levels in the solution. Given the importance of dopamine levels in various neurodegenerative diseases such as Parkinson's and Alzheimer's the sensor is of great medical importance.

In the last five years, the researchers are shifting from the chemical synthesis of nanoparticles to low cost methods using the products of plants such as Chakkota. The objective is to tailor these nanoparticles to specific needs and to ensure that by-products of the

synthesis has no adverse impact on the environment.

Spectrochim. Acta A, Mol. Biomol. Spectrosc., **185**: 11–19

Bricks and Concrete with Sugarcane Bagasse ash in construction materials

Sugarcane is a popular cash crop in India and its products are extensively used in the food and medicine industries. Bagasse, the fibrous remains after juice extraction, is a major agro-industrial waste product, usually burnt and discarded as landfill, causing various environmental problems.



Image: Wikimedia Commons

Last fortnight, a team of researchers from the Indian Institute of Technology Madras, reported advantages in

using sugarcane bagasse ash as ingredient in the manufacturing of construction materials.

The scientists collected bagasse ash samples. And they investigated the effect of alkali-based bagasse ash as binder on curing. Curing involves maintenance of proper temperature and humidity so that the reaction with water leads to crystal growth and strengthens the concrete.

The scientists conducted a performance evaluation on the use of bagasse ash for alkali-activated concrete and unburnt bricks. Sugarcane bagasse ash based concrete had better compressive strength and workability than slag-based geopolymers. The results show significant increase in the strength and durability of bagasse ash blended specimens.

They compared the compressive strength of the specimens, activated using two types of alkali activator solutions: sodium-based and potassium-based. The bagasse ash blended specimens with potassium-based activator performed better than those with sodium-based activator.

The researchers made unburnt bricks with bagasse ash and report that these

had higher strength and lesser weight than fly ash bricks.

Then they made paver blocks with sugarcane bagasse ash and sand. And found that the paver blocks exhibited significant resistance against water penetration and sorption. They were also more durable than similar products.

India ranks second in the world amongst the sugarcane producing countries. The results from this research provide a possibility for sustainable use of a substantial agro-industrial by-product – sugarcane bagasse ash – which otherwise pollutes the environment.

J. Mater. Civ. Engg., **29**(10):
04017189

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ACKNOWLEDGEMENT. Science Media Centre, IISER Pune, for access to scientific databases.

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