Science Last Fortnight

Areca Nut Husk in Drug Delivery

Formation of giant vesicles

Betel-nut, the *Areca catechu* nut, is a prominent crop of India. Its production in the country is the highest in the world. Areca nut husk, a waste product, has hard fibres and has been exploited as an industrial raw material for manufacturing hardboard, paper board, insulation wool and wrapping paper. The cellulose nanofibres of this husk have recently gained attention due to their potential in the preparation of polymer composites with improved properties.

Image: palmpedia.net

Scientists from the CSIR-National Institute for Interdisciplinary Science and Technology, Thiruvananthapuram now report synthesising nanofibrillated cellulose from the husk fibres. They used oleylamine, an unsaturated fatty amine, for this. The oleylamine molecules self-assemble to form giant vesicles in this modified nano-fibrillated cellulose, which, the researchers claim, have immense potential in drug storage and delivery.

To synthesise these vesicles, they extracted cellulose from the husk fibre. They bleached it to remove lignin and washed it with a dilute alkali solution to purify the cellulose. They neutralised the product by washing with distilled water and modified this product by carboxylation. After adjusting the acidity, they added an oleylamine solution for further modification and finally purified it by centrifugation.

The team studied these nanoparticles using conductometric titration, X-ray photoelectron spectroscopy, energy dispersive spectroscopy, transmission electron microscopy, Fourier-transform infrared spectroscopy and dynamic light scattering. These tests confirmed the self-assembly of the modified system into spherical particles, the size of the fibrils and the amidation of the carboxyl groups functionalised with oleylamine.

The researchers prepared solutions of the nano-fibrillated cellulose with tetrahydrofuran for a self-assembly study. And they observed the formation of large vesicles with a diameter thickness of 300–600 nm.

The scientists suggest that the non-polar interactions of the unsaturated long aliphatic chains, stabilised by the intermolecular hydrogen bonding interactions within these modified fibrils, lead to the formation of such giant vesicles.

The scientists claim that these giant vesicles of biocompatible nanomaterials have great potential for applications in the storage and delivery of drugs and cosmetic materials as well as in biosensors.

Carbohydr. Polym., **182**: 62–74

Drug Repurposing for Cancer

Quinoline acetohydrazide derivatives

Developing new drugs is challenging for the pharmaceutical industry – most drugs fail during development and do not reach the market. This means huge expenses without any returns. Drug repurposing – using known drugs and compounds to treat new indications – has a significant advantage over drug development: the drug has already passed through a stringent clinical trial protocol and toxicity tests. This significantly reduces expenses.

Scientists from the Sri Sathya Sai Institute of Higher Learning, Andhra Pradesh and the VIT University, Tamil Nadu now report repurposing quinoline acetohydrazide derivatives. Quinoline derivatives are wide-spectrum antibacterial agents. With azomethine, they become anti-inflammatory and anti-convulsive.

The researchers used computer simulation to study the possibility of repurposing. They used *in silico* molecular docking techniques to predict the preferred orientation of one molecule to another when bound to form a stable complex.

The scientists used a membrane stabilisation study and an enzyme assay to measure enzymatic activity for evaluating the mode of action of the drug.

The entire data set demonstrated the significant anti-cancer and anti-inflammatory activity of quinoline acetohydrazide derivatives. The *in silico* binding affinities are comparable to those of the prescribed standard reference drugs. This suggests their potential role in inflammation and cancer therapeutics.

The scientists consequently confirmed these effects *in vitro*. For clinical applications, however, even the repurposed drug has to pass through further experimental procedures and clinical trials.

J. Mol. Struct., **114**: 437–444

Nanohybrid Doxorubicin Delivery

Heating up cells for cancer therapy

Graphene is biocompatible, cost-effective and has extensive applications in biomedicine. It is non-toxic and an efficient drug nanocarrier. Iron oxide, yet another nanomaterial with paramagnetic properties, is an important marker in cancer research and therapy.

Last fortnight, scientists from the IIT Mumbai, reported using a nanohybrid of graphene and iron oxide to deliver doxorubicin, a widely used anti-cancer drug. The combination, they say, can synergise drug therapy with hyperthermia therapy to manage cancer. A magnetic field, produced by an AC electric current, can create heat in the delivery platform due to the action of iron oxide.

The researchers dispersed graphene oxide by ultrasonication. Then they combined iron oxide salts with the graphene oxide suspension. A series

of chemical treatments produced a crystalline precipitate of the nanohybrid. X-ray diffraction patterns of the nanohybrid showed an arrangement of iron oxide over graphene-stacked sheets.

From transmission electron microscope images, the team observed that the nanohybrids were segregated, and had particle sizes of 8–10 nm. With the help of the Raman spectrum, the team confirmed the functional groups of the nanohybrid. Magnetisation plots confirmed its superparamagnetic property.

For drug loading studies, they screened three varying concentrations of doxorubicin and the nanohybrids and arrived at an optimal ratio. They conducted a drug release assay by scoring HeLa cell viability. Inhibition of cell proliferation *in vitro* indicated sustained release of doxorubicin from the nanohybrid.

On exposure of HeLa cells to the magnetic field of an AC current, the nanohybrid led to maximal cell death, clearly suggesting the synergetic action of the drug delivery system and the higher temperature.

The complex, diverse and heterogeneous nature of tumours has imposed challenges in choosing any single-therapy strategy. Synergistic cancer therapies seem to be more efficient in suppressing tumour progression.

The nanohybrid is versatile in terms of functional group, drug binding-release kinetics and cytotoxicity. The next important step is to target the delivery of the nanohybrids specifically to cancer tissues for effective chemo-thermo cancer therapy.

J. Magn. Magn. Mater., **448**: 332–338

No More Contaminated Water

Antibacterial filter

Polyvinylidene fluoride is an extensively used membrane material for water purification applications. Tethering biocides on the membrane helps increase antimicrobial properties. However, the leaching of such chemicals leads to loss of antibacterial activity and pollution of the environment.

Scientists from the Indian Institute of Science, Bengaluru used a contact-killing approach to create an antimicrobial membrane. Graphene oxide and phosphonium salts are reported extensively for their antimicrobial and antifouling activities. The team facilitated ester bond formation between the membrane surface and graphene oxide. Then they grafted phosphonium salt molecules onto it.

The researchers used Fourier transform infrared spectroscopy to confirm the presence of the characteristic epoxy bond of graphene oxide. They observed a chemical shift in ^{31}P nuclear magnetic resonance spectroscopy which established the presence of phosphorus on the composite. X-ray photoelectron spectroscopy confirmed these findings.

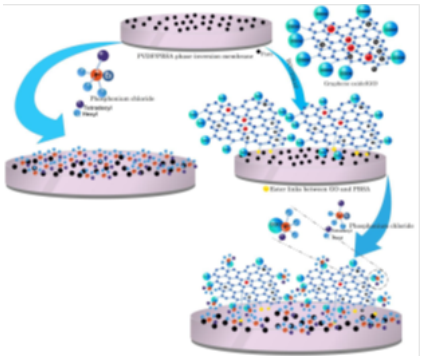
The synergistic effect of graphene oxide and phosphonium salts made the hydrophobic polyvinylidene fluoride membrane hydrophilic. The membrane does not clog easily and allows a stable flux of water due to the pore structure.

The scientists documented reduced contact angle and increased uptake per cent of water flux. They also noted decreased membrane hydraulic resistance and increased trans-membrane flux. This suggests increased affinity of the membrane to water.

High water flux recovery ratio and low irreversible flux decline ratio indicated lower susceptibility of the membrane to bio-fouling. So the team used model coliform strains, *Escherichia coli* (Gram-negative) and *Staphylococcus aureus* (Gram-positive) bacteria, to study the antimicrobial action of the modified membrane. A two-hour treatment, with the modified membrane, showed a seven-fold reduction in bacterial count indicating highly antimicrobial activity.

The team studied the mechanism of the antimicrobial action systematically. They used a hydrophobic fluorescent probe, n-phenyl-1-naphthylamine, for bacterial membrane permeabilisation studies. They noted high probe uptake and maximum leakage of intracellular K^+ ion and nucleic acids in bacterial cells which were in contact with the graphene-modified membrane. They also recorded high fluorescence intensity of dichlorofluorescein in the bacterial cells. Scanning electron microscope images showed punctured holes in bacterial cells attached to the modified membrane. This indicated the presence of a high concentration of reactive oxygen species due to metabolic stress in the bacterial cells. Thus, the membrane modified with graphene and phosphonium derivatives seems to work like a beta lactam antibiotic, making the bacterial cells leaky.

The scientists then performed a long run-time anti-fouling flux experiment. The membrane showed efficient microbial purification even after continuous feed of contaminated water.



The modifications suggested for the membrane surface are simple and effective with excellent fouling resistance, showed impressive reduction of bacterial count and had stable flux performance. Now it will take a synergy between the Water Mission and the Make in India programme to mass produce such membranes.

J. Membr. Sci., **548**: 203–214

Monitoring Mercury

Smart sensor

Mercury is a toxic heavy metal, even at low concentrations. It spreads to unexposed regions, in atmosphere, water and soil through a biogeochemical cycle. Thus, it enters the food chain and poses health problems. Hence, continuous monitoring of the pollutant in the environment is indispensable.

Recently, a team from the JNCASR, Bengaluru and the RMIT

University, Australia designed an ultrasensitive sensor to detect mercury in water. The crucial element of this sensor is a quenching probe for mercury – histidine conjugated perylene diimide. The molecule contains perylene diimide, a fluorescent compound with high quantum yield, with histidine, attached at both ends. This creates a bolaamphiphile structure making this macromolecule more water soluble – a necessary condition for practical applications.

The team prepared a monolayer of polystyrene nanospheres, using electron beam evaporation, on a silica platform as base template for the sensor. Then they deposited gold particles onto the template monolayer. This acted as signal transducer.

The scientists attached histidine conjugated perylene diimide to the surface of the gold particles using one of the histidines. This leaves the other histidine free to take part in the quenching reaction with mercury. Histidine has an imidazole group that chelates with metals. When a green laser was applied, the sensor produced visible fluorescence, if bound with mercury. This can be measured accurately with Raman spectroscopy.

The team tested this sensor with different concentrations of mercury. And found that it can accurately measure mercury concentrations of up to 5 nM – two folds lower than the allowed standard limit of mercury in drinking water. The scientists tested this sensor with other metal ions such as manganese, copper and cadmium also. They found the response of the sensor non-significant. Thus the sensor is specific to mercury.

The mercury bound to the sensor can easily be removed by using cysteine, which sequesters mercury from the histidine. Thus the sensor is reusable.

The scientists claim that this technology is robust and handy. And it enables rapid field detection of mercury at parts per quadrillion concentrations. Now, entrepreneurs can commercialise this technique to mitigate mercury contamination.

Biosens. Bioelectron., **100**: 556–564

Nanocomposite Adsorbents

An effective way to purify water

Rapid industrialisation has contributed to the release of toxic heavy metals into water bodies in India. Heavy metals tend to accumulate in living tissues, causing various diseases and disorders. A report[1] from 2010 indicates that one third of samples collected from selected cities failed to meet WHO standards of safe potable water.

LEAD CONTENT IN WATER:: CITIES AT RISK

ALARMING	HIGH	MEDIUM	LOW
Kolkata	Delhi	Chennai	Bangalore
Kochi	Coimbatore	Ludhiana	Ahmedabad
Mumbai	Madurai	Surat	Hyderabad
Pune	Bhubaneshwar	Ghaziabad	Indore
Nagpur		Jamshedpur	Bhopal
Nashik			Chandigarh
Guwahati			Lucknow
			Mangalore
			Mysore

Among the techniques developed to remove toxic metals such as lead, cadmium, chromium and nickel, adsorption is efficient and fast. Moreover, diverse adsorbents are easily available. Among them, chitosan has emerged as the most promising. Though chitosan has small surface area, low porosity and poor selectivity, studies show that the chemical modification of chitosan with an acidic polymer, such as polymethacrylic acid, improves its adsorbency. Chitosan can also be modified with an inorganic filler to make it a more efficient adsorbent. One such filler is the halloysite nanotube, a naturally occurring clay mineral with nanotubular structure.

Last fortnight, scientists from the University of Calcutta, West Bengal, reported a nanocomposite by integrating chitosan with cross-linked polymethacrylic acid and a nano-sized halloysite nanotube to create an adsorbent that can remove lead and cadmium ions from water[2].

They tested the material for the removal of lead and cadmium ions and report that the composite shows high adsorption. It removes a high percentage of these metals from water as single and as binary mixtures.

Developing the technology will give water authorities more room to be stringent with industries that release heavy metals. Heavily polluted rivers, such as the Yamuna and the Kaveri may, in the near future, get a respite and chances of the availability of safe potable water become brighter.

[1]*LEAD Action News*, **10**(1), June 2010

[2]*Carbohydr. Polym.*, **182**: 159–171

Improving Algal Biodiesel Stability

Binary combination of antioxidants

Biodiesel is a renewable alternative to petroleum diesel. It is easily manufactured by the trans-esterification of edible and non-edible vegetable oils. However, biodiesel has poor storage stability. Oxidising biodiesel leads to the formation of oxidised by-products and reduces engine performance.

To overcome this problem, a team from the University of Petroleum and Energy Studies, Dehradun collaborated with scientists from the Government Post Graduate College Gopeshwar, Uttarakhand, to report a solution: adding binary combinations of antioxidants to algal biodiesel.

'From available literature, we came to know that pyrogallol was the best antioxidant. But to align our research with current trends of biofuel production and processing, we focused on evaluating lower concentrations of binary antioxidants to achieve the best antioxidant synergy for the maximum stabilisation of algal biodiesel' says Girdhar Joshi.

The scientists obtained a culture of micro alga, *Chlorella vulgaris*, from the Vivekananda Institute of Algal Technology, Chennai. They extracted lipids from the micro algae and transesterified the lipids using a base catalyst. After purification, they obtained biodiesel and glycerol, as by-products. The team washed the biodiesel with lukewarm distilled water to remove residual glycerol and purified it by vacuum distillation to get rid of impurities and moisture.

Besides pyrogallol, the scientists used propyl-gallate and tert-Butyl hydroxyquinone as antioxidants. They prepared blends of algal biodiesel with two antioxidants at a time, in different ratios. Then, they stored the samples indoors and periodically

took them out to study the effects of the antioxidants added.

'We observed improvement in the induction period of algal biodiesel with a binary mixture of antioxidants compared to what we found with individual doses of similar concentrations' says Devendra Rawat.

'The binary combinations of 1 : 3 and 3 : 1 by weight of pyrogallol : propyl-gallate showed maximum effectiveness in induction period, stabilisation factor and antioxidant synergy' says Pankaj Kumar.

The team feels that the stabilisation is probably because of the optimum molecular interaction achieved with the 1 : 3 ratios of antioxidants. Further research is required to understand the reason behind the increased effectiveness of the synergy between the antioxidants at the 1 : 3 ratios, says Girdhar Joshi.

However, it is clear that 500 ppm of 1 : 3 binary formulations of antioxidants can be mixed with algal biodiesel for increasing long-term storage. The Ministry of Petroleum and Natural Gas and the Ministry of Agriculture can use this research to popularise biodiesel and to replace petroleum diesel with algal biodiesel in the near future.

Fuel, **214**: 471–479

Degrading Diclofenac

TiO_2 nanocomposite

Environmentally hazardous diclofenac is used as topical pain reliever in small doses. However, due to improper use and disposal, it ends up in aquatic ecosystems. Photocatalysts can be used to enhance the natural photodegradation of diclofenac. To speed up the reaction further, photocatalysts are doped.

Last fortnight, Thiruppathi and team from the Kalasalingam University and the VIT University, Tamil Nadu attempted to use nanocomposites to degrade diclofenac. They synthesised a cerium ion doped titanium nanocomposite by exposing a cerium nitrate and titanium isopropoxide-mixture to high temperature along with sodium borohydride. Then, they characterised the nanocomposite, using X-ray diffraction, and scanning and transmission electron microscope techniques. They found that it had a pristine, closely compacted crystalline nature.

They added the nanocomposite to a diclofenac solution and monitored photodegradation using a UV visible spectrometer. By the end of 80 minutes, the absorbance value reached zero showing that there was complete degradation.

The team went on to test the nanocomposite for stability and reusability. They separated the composite by centrifugation and tested the photodegradation ability again. They report that the nanocomposite is re-usable for five cycles.

They used the nanocomposite in sewage water samples with concentrations from 5 to 25 μM. They observed a reduction in degradation when diclofenac concentration increased beyond 20 μM. The cerium ion-doped titanium nanocomposite performed better than widely used photocatalysts. It is now up to policy makers, corporations and municipalities to effectively use this technology to reduce water contamination by diclofenac.

J. Alloys Compd., **735**: 728–734

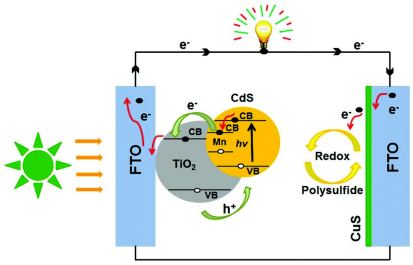
Quantum Dots in Solar Cells

Photovoltaic performance analysis

Researchers are fascinated by the photovoltaic performances of quantum dots – very small semiconductor nanoparticles. The lower costs of producing quantum dot nanomaterials make them an attractive alternative to silicon for producing solar cells. Among the many semiconductor quantum dot nanomaterials reported so far, cadmium sulphide is well suited to solar cell applications due to its lower band gap value – around 2.4 eV. However, the performance varies widely depending on the size of the nano-semiconductor.

Recently, scientists from the SSN College of Engineering, Chennai came up with a technique to identify the optimum size of cadmium sulphide nanoparticles for solar cell applications.

To prepare the samples, they adopted the SILAR method – adding successive ionic layers by means of adsorption in a chemical reaction. By increasing the number of cycles of deposition, from 9 to 12, 15 and 18 cycles, they could get increasing sizes of cadmium sulphide quantum dots. Using X-ray diffraction, they determined that the size of the cadmium sulphide increased from 3 to 9 nm with increase in deposition cycles. The optical properties showed a decrease in band gap with increase in deposition cycle, they report.



Courtsey Dalton Trans., 2015, **44**, 630–638.

By carefully evaluating photovoltaic parameters, including current density and voltage, the team reported an efficiency of 1.8% for the 6.8 nm sized cadmium sulphide quantum dots, prepared using 15 deposition cycles. Beyond this deposition cycle, the particle size and series resistance increases abruptly. Therefore, efficiency decreases.

This research is an innovative step towards developing solar cells with the right sized quantum dots. However, though the efficiency of the cadmium sulphide nanomaterial reported is relatively low, its photostability, ease of fabrication and low cost make it attractive for solar cell applications.

J. Alloys Compd., **735**: 202–208

Reports by: **Sanghamitra Deobhanj, Sileesh Mullasseri, S. Suresh Ramanan, K. S. Nitin, S. Balaji, K. V. Srividhya, Mridula Vellore, Nivedita Mishra** and **P. Gowdhaman**

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scienceandmediaworkshops@gmail.com