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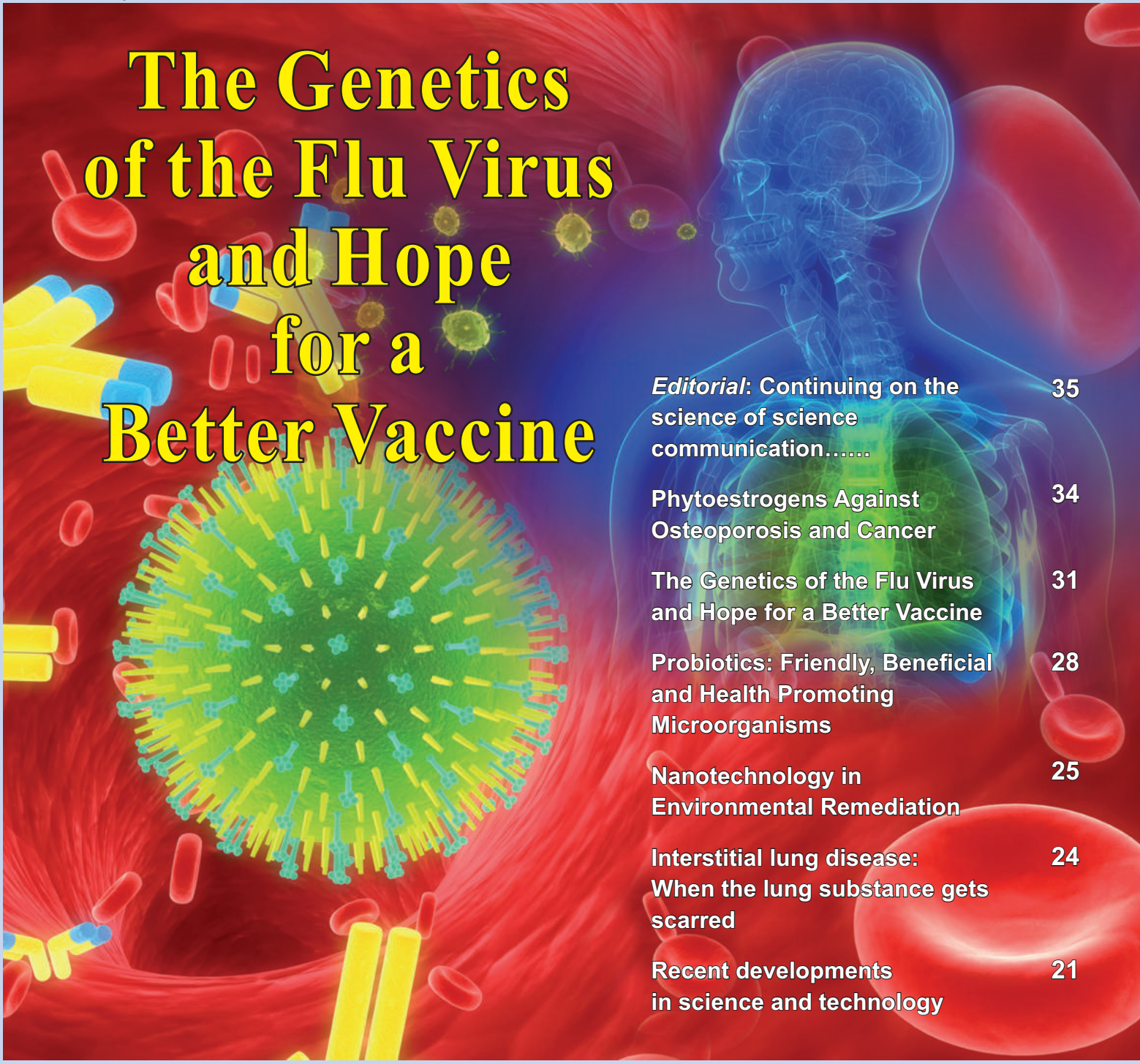

The Genetics of the Flu Virus and Hope for a Better Vaccine

... think scientifically, act scientifically... think scientifically, act scientifically... think scientifically, act...

Continuing on the science of science communication……

Dr. R. Gopichandran

Some of the best deliberations in the field of science communication are undoubtedly of the national academies of engineering, science and medicine in the United States of America. This is clear when we follow the insights they present through their coming together, and a typical case in point is of the 2013 colloquium[1]. Quite obviously they recognise the need to value perceptions pubic carry about science, and circumstances that determine such perceptions. This approach is quite inclusive and therefore creates the case for science communicators to not pre-judge or condemn sections of pubic as unscientific. Especially so when circumstances are not understood through a holistic perspective. The summary ups the ante citing "...people are not idiots...". It gravitates towards the need to therefore use such methods/approaches to communicate science that have reasonably good chances of success. This is reportedly possible when communication teams are well represented with people with adequate abilities to address complexities across and within disciplines. Science communication by itself is therefore not a monolith.

The 2016 research agenda meeting[2] (cited in an earlier editorial too) has addressed the modalities of science communication. The parameters stated reflect a well-defined logical framework; almost a caveat at less informed strategies/ attempts that trivialise science communication. Varner[3] delivers a profound message for communicators to "…communicate science with the same rigour as the science we wish to share…". This is almost corroborated by Kahan[4] with an additional take on such aspects as freedom and pluralism as the founding principles of diversity in perceptions.

The report on Public Attitudes to Science[4] presents interesting insights on the dynamics of science communication and establishes the variegated landscape of perceptions and their determinants. The most important take away, based on the insights derived from the cited sources is for communicators and institutions engaged in science communication in India. It is about a much felt need for empirical evidences about such diversities in the Indian context. Importantly, the questions to be administered as part of reality checks that will document and interpret evidences should not harbour pre-conceived notions about perceptions. More so, is the safeguard for zero-bias in interpreting empirical evidences.

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Email: r.gopichandran@vigyanprasar.gov.in ■

Editor	:	R Gopichandran
Associate editor	:	Rintu Nath
Production	:	Manish Mohan Gore and Pradeep Kumar
Expert member	:	Biman Basu
Address for correspondence	:	Vigyan Prasar, C-24, Qutab Institutional Area, New Delhi-110 016 Tel : 011-26967532; Fax : 0120-2404437 e-mail : info@vigyanprasar.gov.in website : http://www.vigyanprasar.gov.in

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Phytoestrogens Against Osteoporosis and Cancer


Prof. Dhan Prakash Dr. Charu Gupta
E-mail: dprakash_in@yahoo.com

Phytoestrogens are non-steroidal oestrogen-like chemical compounds produced by plants and present in many natural dietary sources, such as soybeans, wheat, barley, corn, alfalfa, and oats. They mimic mammalian oestrogens and therefore are considered to play an important role in the prevention of cancers, heart diseases, menopausal symptoms and osteoporosis. Oestrogens influence the growth and functioning of female and male reproductive tissues, maintain the skeletal and central nervous system, have protective effects on heart and protect against colon cancer and aging of skin. Plants with oestrogen-like biological activity are being used in traditional systems of medicine and folklore, for example, the pomegranate is associated with fertility; the Thai vine, *Pueraria mirifica*, is considered a rejuvenator and aphrodisiac; and hops was believed to lower libido by the German clergy in the middle ages. Till now, several hundred plants have been found to exhibit oestrogenic activity due to the presence of phytochemicals called phytoestrogens. They are recommended for the prevention of disturbed hormone related diseases.

Phytoestrogens are substances that promote oestrogenic actions in mammals and are structurally similar to mammalian oestrogen 17β-oestradiol. The diverse biological activity of phytoestrogens is due in part to their ability to act as oestrogen agonists and also as antagonists. They can mimic endogenous oestrogens and cause oestrogenic effects. As oestrogen antagonists, they may block or alter oestrogen receptors and prevent oestrogenic activity.

Phytoestrogens are able to interact with enzymes and receptors, and because of their stable structure and low molecular weight they can pass through cell membranes. These interactions allow them to bind to oestrogen receptors, induce specific oestrogen-responsive gene products, interfere with steroid hormone metabolism or action and alter oestrogen receptor structure and affect transcription. The different activities and the bioavailability of phytoestrogens vary depending on such factors as the form of administration, dosage, individual metabolism and the ingestion of other pharmacological substances. Target tissue, concentration dependency, number and type of oestrogen receptor and the presence or absence of endogenous oestrogens also influence the effect of phytoestrogens.

There are several classes of phytoestrogens, which include steroidal oestrogens, found in a few plants and the more ubiquitous phenolic oestrogens like isoflavones, stilbenes, coumestans and lignans. Other classes of phytoestrogens that have been reported include: anthraquinones, chalcones, flavones, prenylflavonoids and saponins. Phytoestrogens have been categorised based on their chemical structures, which resemble 17β-oestradiol. Oestrogen receptors bind with steroidal as well as numerous non-steroidal compounds. An aromatic ring and a hydroxyl group are important for binding effectiveness and the remainder of the oestrogen receptors will accept hydrophobic groups.

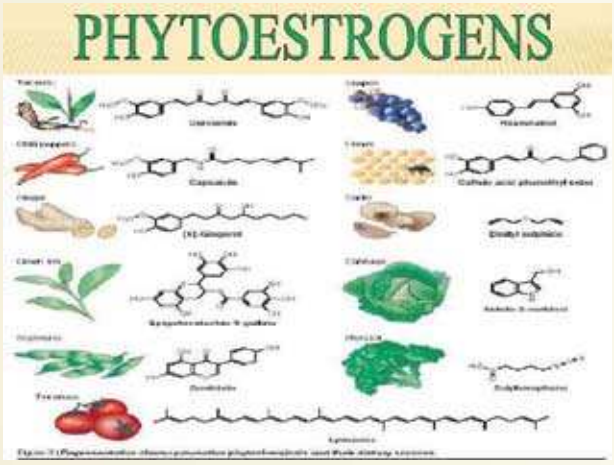
The mechanisms through which the phytoestrogens may influence sex hormone production, metabolism and biological activity could depend, at least in part, on their mixed oestrogen agonist/antagonist properties and binding to oestrogen receptors. Furthermore, these weakly oestrogenic molecules have been demonstrated to affect intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, cell differentiation, cell adhesion, formation of new blood cells, and programmed cell death. Experimental studies in animals suggest that both lignans and isoflavonoids are among the dietary factors that afford protection against atherosclerotic vascular disease and cancer. The biological activity of individual phytoestrogens varies and is often reported as less active than mammal or synthetic oestrogens. Differences in oestrogenic activity of similarly classified chemicals may be due to the structural features or deviations in those structures.

The naturally occurring groups of phytoestrogens

The major phytoestrogens groups are isoflavones, flavones, stilbenes, lignans and coumestans (Table 1). As studies continue to evaluate the biological effects of phytoestrogens on human health, the complexity is more evident as oestrogenic and anti-oestrogenic effects are observed as well as a variety of mechanisms of action.

Table 1: Dietary sources of phytoestrogens of human interest

Class of phytoestrogens	Food sources
Isoflavones	Soybean, peanut, clover, sunflower seed, walnut
Flavones	Parsley, celery, citrus peels, capsicum, pepper
Stilbenes	Grape, peanuts
Lignans	Soybean, peanut, broccoli, cashew nut, kiwi, pomegranate, triticale straw, flaxseeds, cereals
Coumestans	Mung beans or soybean sprouts, alfalfa sprouts, clover



soy such as soy-based infant formulas, tofu, soymilk, soy flour, textured soy protein, soy protein isolates, and tempeh as well as over-the-counter dietary supplements. Genistein is a phytoestrogen that binds to oestrogen receptors and has both weak oestrogenic and weak anti-oestrogenic effects. *In vitro* studies have shown that the growth of both oestrogen receptor-positive breast cancer cells and oestrogen receptor-negative breast cancer cells is inhibited when high levels of genistein (>10μM) are added to the culture medium. Genistein has consistently been shown to inhibit the development of oestrogen-sensitive mammary tumours when given to pre-pubertal rats.

Isoflavones such as genistein found in soybean should be an integral part of everyone's diet. They help to reduce cholesterol, prevent atherosclerosis, protect or slow prostate and breast cancer growth, prevent the kind of cell mutation that causes DNA damage, inhibit blood supply to already existing tumours, ease menopause and lower the risk of osteoporosis. Genistein is considered the natural analogue to the drug tamoxifen, which is an anti-oestrogen compound used to treat breast cancer. Genistein has also shown the ability to destroy certain cancer gene enzymes that can change a normal cell into a cancer cell, which simultaneously inhibit blood vessel growth to larger tumours. Genistein can diminish the possibility of cellular mutations which can result in malignant tumours, especially in tissue which is oestrogen-sensitive.

A closely related compound to the isoflavonoids is 8-prenyl-naringenin, an isoflavanone found in hops (*Humulus lupulus*), an ingredient used in beer. Populations in China, Japan, Taiwan and Korea are estimated to consume high quantities of isoflavanones and women of these countries complain fewer incidences of osteoporosis and related health problems, especially hot flushes, cardiovascular diseases, lower incidence of hormone dependent breast and uterine cancer.

Isoflavones

These are the most studied group of phytoestrogens. These are found exclusively in the family Fabaceae (Leguminosae). Soybeans are a very rich source of isoflavones and contain approximately 2 grams of isoflavones per kilogram of fresh weight. The isoflavonoids encompass several structurally and biosynthetically related classes such as flavonols, anthocyanins, flavanones, coumestans, and chalcones. Isoflavones have a structure similar to oestrogen and have the capacity to exert both oestrogenic and anti-oestrogenic effects, they may block the effects of oestrogen in some tissues, e.g., the breast and womb lining but act like an oestrogen in providing possible protection against bone loss and heart diseases.

Isoflavones can reduce the effect of the oestrogen on cells and skin layers when the hormone levels are high, and then essentially reduce the risk of oestrogen-linked cancers. Some isoflavones are termed as antioxidants because of their ability to trap singlet oxygen. Some isoflavones, in particular soybean isoflavones, when studied in populations eating soybean protein, have indicated that there is a lower incidence of breast cancer and other common cancers because of its role in influencing sex hormone metabolism and biological activity. Their main sources (Table 1) are soy cheese, soy flour, soy bean, tofu and legumes.

Genistein is one of the several known isoflavones. It is found in a number of plants including lupin, fava beans, and soybeans. Soybeans, a cholesterol-free, high-protein legume, contain the most genistein. Other legumes, such as chickpeas, contain small amounts. Genistein can be found in many food products containing

Flavones

The flavones are a group of naturally occurring chemical compounds widely distributed in plants. Natural flavones include apigenin, chrysin, quercetogetin, luteolin, and tricetin. Their major sources are parsley, celery, citrus peels, capsicum, and pepper. Apigenin is commonly present in fruits and vegetables with proven anti-inflammatory and anti-carcinogenic effects in various animal tumour model systems. It has been shown to suppress the formation of new blood vessels in melanoma and carcinoma of the breast, skin, and colon. Apigenin has shown potential to inhibit growth in several types of human cancer cells, including breast, colon, skin, thyroid, leukaemia, and prostate cancer. These cell inhibitory effects are mediated via cell cycle arrest and induction of apoptosis.

Stilbenes

An example of stilbene is resveratrol found in black grapes which has several health benefits. It exists in two structural isomeric forms, *cis* and *trans*, with the trans form being more common and possessing greater biological activity. One of the richest sources of resveratrol is *Polygonum cuspidatum*, a weed that is used in traditional Chinese and Japanese medicines. Trees such as Eucalyptus and spruce have also been found to contain resveratrol. The primary sources in the human diet are peanuts, black grapes and red wine.

The potential health benefits of resveratrol include its antioxidant, cardio-protective, chemo-preventative, anti-inflammatory, and estrogenic properties. The antioxidant activity of resveratrol may also be associated with protection against the progression of atherosclerosis. Red wine is one of the few dietary sources of resveratrol and it is believed that this compound is responsible, in part, for the positive cardiovascular effects associated with moderate wine consumption. The oestrogenic activity of resveratrol may also help prevent bone loss in post-menopausal women. Resveratrol has been shown to exert neuro-protective effects, as well as beneficial effects on the cardiovascular system.

Lignans

The lignin family is a large group of naturally abundant molecules that can be found in a plethora of plants. Flax seed is a particularly rich source. Lignans, along with isoflavones and coumestans, comprise the three major classes of phytoestrogens. When plant

lignans are consumed, intestinal bacteria convert some into two mammalian lignans, enterolactone and enterodiol. These compounds are absorbed from the digestive tract, circulate and are excreted in the urine.

Due to the structural similarity of lignans found in the stomach with mammalian oestrogens, these compounds are potentially interesting for combating some hormone-dependent cancers. Some epidemiologic investigations have shown that the risk of breast, prostate and colon cancers is lower in countries or regions in which the diet is particularly rich in lignans. Their antioxidant activity is also one of the possible anti-carcinogenic mechanisms of the compounds.

Coumestans

Coumestans are an important group of plant phenols that show oestrogenic activity. The main coumestans with phytoestrogenic effects are coumestrol and 4′-methoxycoumestrol. Coumestrol has been reported to inhibit bone resorption and to stimulate bone mineralisation. Coumestans are less common in the human diet than isoflavones yet similar to isoflavones, in that they are also found in legumes, particularly sprouts of alfalfa and *mung* bean (*Vigna radiata*) and they are especially high in clover. Soybean sprouts also show high levels of coumestrol (71.1µg/g). However, low levels have also been reported in Brussel sprouts and spinach.

Human health benefits of phytoestrogens

Researchers have proposed that lower cardiovascular diseases, osteoporotic fractures and rates of breast cancer in Asian populations are related to a diet rich in soybean products or, in other words, phytoestrogens. Several studies have discussed the potential effects of phytoestrogens in treating breast cancer, prostate cancer, endometrial cancer and liver disease.

1. Breast cancer

Epidemiological studies of breast cancer and the dietary intake of soy and lignin have been reviewed, as well as the mechanisms of phytoestrogenic action in breast tissue. One task has been to find an oestrogen replacement therapy for women at risk for breast cancer or who have survived breast cancer. A diet rich in phytoestrogens has been suggested as a preventive agent against breast cancer. Prior to menopause when there is a high-oestrogen environment, phytoestrogens may protect against breast cancer and after menopause when there is a low oestrogen environment they may stimulate breast cancer.

2. Prostate cancer

In vitro studies using human prostate cancer cells have shown the inhibition of cell growth with high concentrations of phytoestrogens. Rats consuming soy and rye bran had delayed growth of implanted prostate tumours. Several epidemiological studies suggest the beneficial use of phytoestrogen-rich diet in reducing prostate cancer. Other studies have evaluated alternative therapies, such as soy, black cohosh, vitamin E and red clover for their potential use in alleviating hot flashes for prostate cancer patients.

3. Cardiovascular diseases

After menopause, the risk of coronary heart disease greatly increases due to the loss of oestrogen. Lipid profiles, vascular reactivity, cellular proliferation and thrombosis are factors that affect coronary heart disease on which phytoestrogens have shown beneficial effects.

4. Osteoporosis/bone health

Osteoporosis is often associated with menopause. The evidence supports oestrogen replacement therapy in the prevention of osteoporosis in postmenopausal women and therefore, phytoestrogens have been evaluated for their effects on bone mineral density. Researchers hypothesise that a diet rich in isoflavones has a protective effect on bone. Ipriflavone, a synthetic isoflavone derivative (7-isopropoxy-isoflavone), has been used extensively in animal and human studies to evaluate bone health and phytoestrogens with beneficial results. Genistein, a natural phytoestrogen found in soy bean, has a beneficial effect on bone mineral density. In three different studies on bone mineral density with phytoestrogen consumption conducted with postmenopausal women, showed an increase in bone mineral density. The mechanisms include preventing urinary calcium loss, beneficial effects on osteoblasts, and influence on the secretion of calcitonin which suppresses bone resorption.

5. Menopausal symptoms

The symptoms associated with menopause may cause many women to seek medical care. Hormone replacement therapy has proven effective in the reduction of hot flushes, yet it is still controversial if it may be associated with increased risks of breast and endometrial cancers. Initial findings from randomised controlled trials have shown an increased benefit. Several reviews have discussed studies conducted on phytoestrogens and menopausal symptoms, but still much contradictory evidence exists as to the benefits of phytoestrogens.

6. Cognition

Cognition and memory functioning have been reported to decrease around menopause, and therefore, studies have investigated the association of oestrogen replacement therapy and cognition, as well as phytoestrogens and cognition. However, limited studies are available on the effects of phytoestrogens on cognitive functioning. The mechanisms are not understood, but it has been suggested that phytoestrogens act as oestrogen agonists and may increase spine density and synapse formation in the hippocampus of adults.

Herbal sources of phytoestrogens

Even though they are also found in grains, vegetables and fruits, there is a higher concentration of phytoestrogens in legume plants. The most common phytoestrogen

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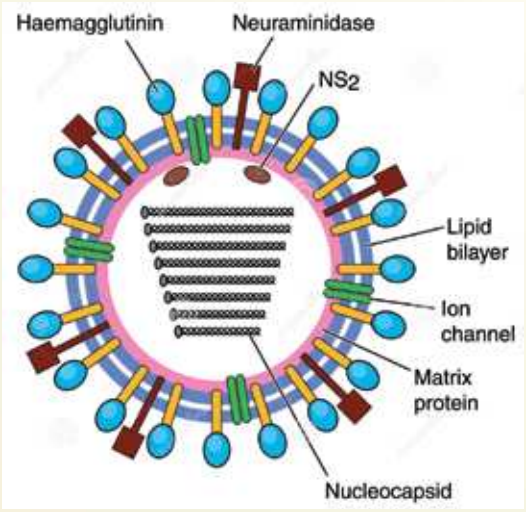
The Genetics of the Flu Virus and Hope for a Better Vaccine

Dr. Ashesh Nandy
E-mail: anandy43@yahoo.com

Influenza, commonly referred to as the 'flu', is a recurrent seasonal infectious disease caused by the influenza virus. Runny nose, mild to high fever, muscle pains, headache, coughing and sneezing are the usual symptoms which generally fade away in 7 to 10 days. During the onset of the disease it spreads through the air from the coughs and sneezes and can infect others nearby through inhalation of the aerosol carrying the virus or by touching contaminated surfaces. If the flu affects a wide cross-section of the population it would be termed an epidemic. Such epidemics occur every year and affects 3 to 5 million people leading to deaths of about 5 to 10% of the infected people from direct (pneumonia) and indirect (respiratory ailments, cardio-vascular diseases) causes. Occasionally, about once every few decades, the virus develops into a pandemic variety striking across the world with fatalities in the millions, the most recent example being the swine flu pandemic that broke out in 2009. Frequent washing of hands with soap during the flu season can prevent infection since the virus is deactivated by soap, but the fact that flu epidemics occur regularly shows that the virus is a persistent beast indeed. Several drugs have been developed over time that can act against the infections, but the virus often becomes resistant to the drugs and new ones have to be developed. This article seeks to explain some of the reasons behind it.

History of influenza

Influenza has been recognised for long as one of the deadliest of infectious diseases. Early historical evidence is scanty, but reports of possible influenza outbreak can be found in Greek writings of 5th century BC. Influenza epidemics in the 12th, 14th and 15th century were chronicled in Europe and in 17th century in America and Europe, with more thorough and quantitative data available from the 18th century onwards. However, it was only in 1932 that the influenza virus was isolated, and since then this infection could be recorded and confirmed by laboratory tests Nevertheless, the severity of the disease was unmistakable: the 1918 Spanish flu pandemic that swept the globe causing over 50 million deaths has been identified recently as one form of the influenza virus. Since then there have been an Asian flu pandemic of 1957-58 and a Hong Kong flu pandemic of 1968-69 causing about a million deaths each. A swine flu pandemic that started in 2009 and swiftly spread across the globe caused lesser fatalities, due perhaps to better preparedness by the nations, but is still popping up in different places, most recently in India in 2015 where it has caused more than a thousand deaths. Seasonal flu is relatively harmless, but nevertheless leads to several thousand direct and indirect casualties every year.



Influenza virion structure

The influenza genome

Such catastrophic events require prompt and effective response and most governments around the world are in different states of readiness with antidotes, vaccines and drugs. But there is a structural issue that is at the root of the problem: viral mutations, for which we need to understand the genetics of the influenza virus. The basic building block of an organism is the DNA molecule; for simple, life forms such as viruses, some can have RNA instead. These complex molecules are built out of four simpler organic groups called nucleotides or bases: adenine (A), cytosine (C), guanine (G) and thymine (T) for the DNA; in the RNA there is uracyl (U) instead of thymine. The final DNA or RNA molecule carries long sequences of these nucleotides. stitched together according to certain rules, which code for different proteins. Viruses can have a few thousands of these bases, mammalian DNA can contain billions of them. The DNA molecule is an integral part of a cell and contains code to make enzymes and proteins which are the building blocks of, say, hair and skin and eyes and so on. The parts of the DNA that code for proteins are called genes; the human DNA is 3.5 billion bases long and is estimated to code for 30,000 proteins. The entire DNA consisting of all genes is called the genome. The genomic DNA gets replicated when a cell divides making further copies of it – a process known as cell division.

Influenza is a RNA virus that occurs in three types – influenza A, B and C, of which influenza A is the most virulent. The viral genome is around 13,000 bases long, segmented into 8 genes that code for 11 proteins, of which the most important ones, for our purposes, are: hemagglutinin (HA in short), neuraminidase (NA), and polymerase PB1 and PB2. The RNA genome is enclosed in a roughly spherical viral envelope where the HA and NA proteins are located on the surface. The virus particle, called a virion, is made from many proteins and carries several HA and NA on its surface. During infection a part of HA, called the active site, attaches itself to a specific molecule, sialic acid, of the cell of the host animal and then the entire virion fuses itself into the cell. There the virion releases its genes which use the replication and protein making machinery of the host cell to make many more copies of itself. When the new viruses are assembled, the neuraminidase (NA) of each virion uses its own active sites to make it possible for the progeny to be released, after which the cell dies. The newly released virions then proceed to infect other host cells.

Remedies

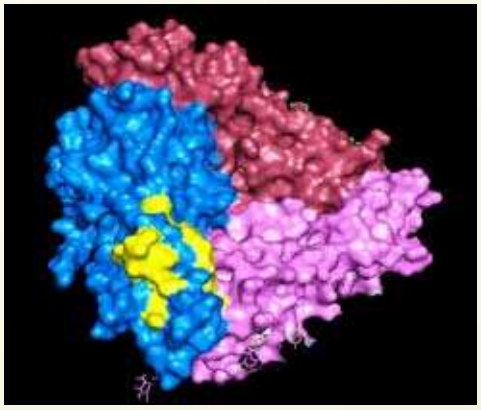
There are two way to fight the infection: drugs and vaccines. Drugs stop the spread of an infection by interfering with its growth or replication. In the case of influenza, drugs such as amantadine and rimantadine were devised to prevent breakup of the virion in the host cell and zanamivir (tradename Relenza) and oseltamivir (Tamiflu/Antiflu) that inhibits the neuraminidase from releasing the progeny virions by blocking its active site by attaching a small molecule inside. Oseltamivir has been extensively used in the case of swine flu pandemic and have been stockpiled for use in case of future epidemics and pandemics.

Vaccines work by enhancing the body's natural defences to prepare against invading germs. The body of an animal contains certain mechanisms (immune system) to protect itself against such unwanted guests. One of the mechanisms is production of antibodies. When a foreign particle, such as a virion, enters a body, certain special cells identify the invaders and organise creation of new molecules whose job is to go and attach themselves to specific parts of the invader and thereby arrange to kill them. The soldiers of the new army are called antibodies and the identified parts of the invaders are called antigens (for antibody generators). Not all parts of the invader are suitable as antigenic sites, but only those that fit a category called epitopes (the sites on the surface of an antigen molecule to which an antibody attaches itself) are suitable. Antibodies are unique to each antigen; once antibodies to some antigens have been created, the next time such an antigen enters a host the antibodies are immediately generated and the invaders swiftly annihilated. This is why some diseases like measles affect an individual only once; on second infection the invaders are immediately recognised and destroyed. This is also the rationale behind vaccines: a part of the disease-causing germ is intentionally introduced into a human or an animal body to generate antibodies so as to be prepared against the real thing.

Viral mutations and drug resistance

The above-mentioned mechanism should have worked very well for influenza also, but there is a twist in the tale. For the antibodies to work the target proteins should be on the surface of the invading particle. So the surface-exposed hemagglutinin and neuraminidase proteins of influenza virion with antigenic sites on their own surfaces are the natural targets. Unfortunately for us, the viruses' genetic makeup sometimes creates problems. In general, when DNA or RNA is replicated in a cell, one or more polymerase enzymes do the job with extremely high fidelity; however, once in a while an error does creep in; e.g., a cytosine in the original is replicated to an adenine in the copy. To prevent such mistakes the cells usually carry error correcting mechanisms that ensure high fidelity of the copied product. But sometimes errors still go through

The influenza virus genome does not have any machinery for error correction, nor can it use the host cell's machinery for this



3D structure of neuraminidase protein (from A Ghosh, A Nandy and P Nandy, BMC Structural Biology 2010, 10:6)

purpose. Replication errors therefore occur very frequently – about one in every 50 to 100 thousand base replications. In other words, one in every ten copies of the genome will, on average, carry an error. This is known as a mutation. Some mutations may change the antigenic site, some may cause a change in the active sites of the HA or the NA, which may then affect the functioning of the drug or the antibodies. However, the mutations occur at random, and since the antigenic segment or the portion containing the active site is only a fraction of the total genome, most mutations will not affect the functioning of the drug or the antibodies, which will destroy the susceptible viruses. But the viruses that get mutations in the antigenic or the active sites can remain unaffected and render the drugs and vaccines ineffective. These viruses are then said to have developed 'resistance' against these drugs and vaccines. This has been the case with the antiviral drug amantadine; there is high level of resistance against another antiviral drug oseltamivir in Japan and there are reports of significant increase in resistance in the USA too.

Mutations in the flu viruses are so numerous that vaccines developed for one year usually require close monitoring and alterations for use in the following year. Centres for Disease Control and Prevention (CDC) in the USA puts out a notice on this every year citing its recommendations. Variations in the genomes from such mutations accumulate at a slow rate and are known as genetic drift. Once a mutation event occurs and the new genome sustains in the long run, the new virus can be specifically identified. The HA and NA have been categorised by their established antigenic sites: To date there are 18 known variants of HA and 9 variants of NA and the viruses are classified according to the particular variant of the HA and NA they contain. Thus we have the H1N1 swine flu, the H5N1 bird flu, the H3N2 flu, the H7N9 flu, and so on. New mutations in antigenic sites of HA and NA could lead to further additions to this table of flu variants.

There is another process of alteration in the flu genome, commonly referred to as genetic shift, which may lead to emergence of new subtypes of the virus. If these subtypes happen to be stable and survive to produce adequate progeny of their own, we will find new subtypes of influenza virus circulating in the environment.

Designing new vaccines

It is no wonder that given these possibilities of continuous genetic drifts and shifts, drugs, and more particularly, vaccines suffer from rapid obsolescence. Clearly a broader approach that attacks the fundamentals of the influenza virus is required to combat the menace, and several universal vaccines are under various stages of development. We could approach the issue by investigating what would be the features of the flu virion that remain constant over the many mutations and whether that could yield any effective approach towards its control. Specifically, one could consider highly conserved surface proteins of the virion and target surface exposed peptides, i.e., short segments of the protein sequences to incapacitate the viral processes by vaccines.

The developments in the fields of immunogenomics and bioinformatics have

shown a new path to vaccine design. In breakthrough exercises on computer-aided vaccine design using the new technique of graphical representation and numerical characterisation of nucleotide and amino acid sequences, this author and colleagues have identified several highly conserved, surface situated segments that can be targeted for peptide vaccine development against neuraminidase protein of the influenza-A virus and the VP7 protein of rotavirus. Peptide vaccines are drawing increased attention due to several advantages: Such vaccines are considered safer than vaccines from bacterial cultures or attenuated or inactivated viruses, and offer advantages such as relatively easier production processes and chemical stability. Synthetic peptide vaccines offer the additional advantage of correcting for antigen fragments exhibiting autoimmune response, high level of standardisation, possibility of conjugation of various peptides from different antigens to the same carrier, and also allow for custom-designed modifications for improved vaccine delivery and rational vaccine design.

Influenza, as one of the outstanding killer diseases with its variability, remains as lethal today as ever before and is likely to be so in the foreseeable future unless new therapeutics can be devised and brought to market fairly rapidly. Here rational peptide vaccine design may hold the key: Given adequate resources of sequence data, the time taken and costs incurred in computer designed peptide vaccines to migrate from lab to field and coupled with their effectiveness, peptide vaccines appear much more advantageous compared to traditional methods and can be considered favourably for pursuing in the twenty-first century.

Dr. Ashesh Nandy is with the Centre for Interdisciplinary Research and Education, 404 B Jodhpur Park, Kolkata 700068.

Phytoestrogens Against Osteoporosis and Cancer *(Continued from page 32)*

found in legumes is isoflavonoids. Soybean, licorice, red clover and flax seeds are good sources of phytoestrogen. Soybean (*Glycine max*) is a good source of genistein, its glycosides and daidzein which are with estrogenic activity.

Flax (*Linum usitatissimum*) seeds contain several substances that are thought to reduce the risk of hormone-dependent cancers, and cardiovascular diseases. Flax seed oil contains polyunsaturated fatty acids such as α-linolenic acid, which may lower cholesterol and have antioxidant effects for health.

Red clover (*Trifolium pretense*) is a legume rich in isoflavonoid phytoestrogens including genistein, daidzein, formononetin and biochanin-A, phytochemicals that are now recognised for supporting critical hormone levels without having any negative side effects. Controlled clinical trials show that phytoestrogens from red clover help to maintain proper bone density in menopausal women, as well as relieving hot flushes and night sweats.

Hops (*Humulus lupulus*) have been valued as a sedative, for inflammation and as a tonic. Menstrual disturbances were frequently observed in women hops pickers and their oestrogenic activity was associated with the plant. The female flowers of hops are considered oestrogenic. The most potent phytoestrogen in hops is 8-prenylnaringenin (8-PN), which is found in beer in low quantities.

Dong quai (*Angelica sinensis*) has been referred to as the 'female ginseng' and is used for a variety of conditions such as a blood tonic and decongestant for body organs. Its roots are used for women as a tonic often in combination with other herbs. Other women's conditions treated with dong quai are dysmenorrhoea, irregular menstruation, constipation, anemia, and abdominal pain.

The root of licorice (*Glycyrrhiza glabra*) has been consumed for thousands of years in China and India for its health benefits and detoxification effects as well as its use as flavouring and sweetening agent. Medicinally it has been used as a demulcent, expectorant and has been shown to have antioxidant and antimicrobial activity. The main components of licorice are glycyrrhizin (glycyrrhizinic acid), which is sweeter than sugar, and glycyrrhetinic acid. Both have been clinically used in the treatment of hyperlipidemia, allergic inflammation, atopic dermatitis and atherosclerosis. The phytoestrogens in licorice have a mild oestrogenic effect, making the herb potentially useful in easing certain symptoms of premenstrual syndrome, such as irritability, bloating and breast tenderness.

Conclusions

Diets rich in plant-derived products may supply a variety of phytoestrogens capable of producing a range of pharmacological effects in the human body. As people live longer, women are spending more of their lives after menopause, affected by a variety of oestrogen-related conditions such as osteoporosis, cognitive and cardiovascular disease, increased risk of breast cancer and other symptoms that decrease the overall quality of life. Epidemiological evidence and experimental data from animal studies are highly suggestive of the beneficial effects of phytoestrogens on human health.

Prof. Dhan Prakash and Dr. Charu Gupta are with Amity Institute for Herbal Research and Studies, Amity University-UP, Sector-125, Noida-201313

Probiotics: Friendly, Beneficial and Health Promoting Microorganisms

Dr. Preeti H. Dave
E-mail: preetidietcare@gmail.com

When we think of bacteria, we consider them as a foe. It is a general belief that bacteria are always harmful. Most people believe that consuming edibles loaded with bacteria would invariably lead to disease and illness. Indeed it is hard to believe that some bacteria could be friendly, useful and health boosters. But there are friendly and health promoting bacteria, which are known as 'Probiotics'.

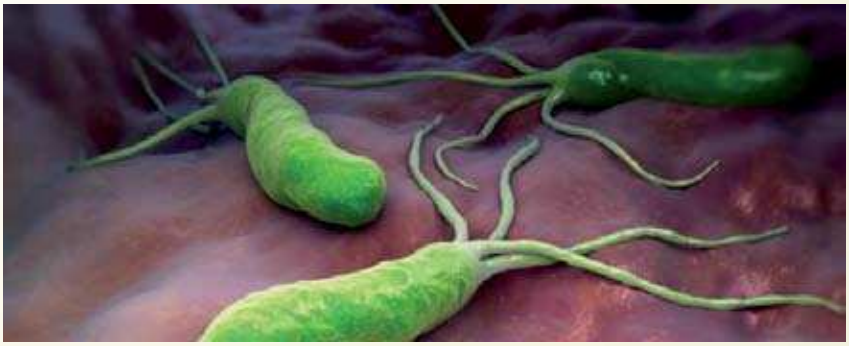
What is a Probiotic?

The word probiotic is actually an admixture of two words: the Latin preposition *pro* (meaning "for") and the Greek adjective *βιωτικός* (biotic), the latter deriving from the noun *βιος* (bios, meaning "life"). This means probiotic means "for life". Probiotic organisms are live microorganisms beneficial to the host organism. World Health Organization (WHO) has defined probiotics as "Live microorganisms which when administered in adequate amounts confer a health benefit on the host".

Our normal intestinal flora contains 100 trillion organisms from 400 different species! It appears unbelievable but is true! Some of these microorganisms are beneficial to us while others are pathogens which cause diseases and discomforts to humans. On the one hand, probiotic organisms suppress the growth of pathogens in the intestine while on the other hand they help the beneficial microbes to flourish. Thus, presence of sufficient probiotics in our gut ensures in maintaining overall health.

Since probiotics are live microorganisms, it is necessary to take them in live condition so as to enable them to flourish inside our intestine. Probiotics are usually consumed as part of fermented foods with specially added active live cultures, as are found in yoghurt, curd, buttermilk, *lassi*, fermented soy milk, and ice cream.

Leading food manufacturing companies and dairies in India have launched number of probiotic products in the market. Probiotic products have also attracted the concern of consumers, especially those who are health and nutrition conscious.



Pathogen present inside the gut.

History of probiotics

Russian scientist and Nobel laureate Élie Metchnikoff was a professor at the Pasteur Institute in Paris. In the beginning of 20th century he observed that gut microflora (bacteria which lives in our intestine) can be modified and harmful microorganisms can be replaced with useful microorganisms by administration of specific useful live microorganisms along with food. The concept of probiotics evolved with Elie Metchnikoff's hypothesis that the long and healthy lives of Bulgarian peasants were the result of their consumption of fermented milk products and yogurt. These fermented milk products contained friendly bacteria which promotes gut health.

Henry Tissier was another scientist who also worked at the Pasteur Institute. He isolated bacteria named *Bifidobacteria* from a breast-fed infant. Tissier discovered that bifidobacteria are dominant in the gut flora of breast-fed babies and they replace some proteolytic (protein-breaking) bacteria that cause disease. He also found that diarrhoea in infants can effectively be treated with bifidobacteria.

In 1953 German bacteriologist Werner Kollath introduced the word 'probiotics' for the first time. This word was used in contrast to the word antibiotic. Antibiotics suppress the growth of microorganisms while probiotics stimulate the growth of friendly microorganisms.

Beneficial bacilli growing on the gut surface.

Which microorganisms are used as probiotics?

Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics. Sometimes certain yeasts and bacilli may also be used. *Lactobacillus rhamnosus*, *Lactobacillus casei*, and *Lactobacillus johnsonii* are the most commonly used probiotic bacteria. These lactic acid bacteria are believed to have beneficial properties. Most of commercial fermented and non-fermented foods, dairy products are made up with probiotic strains of *Lactobacillus, Bifidobacterium* and *Streptococcus.*

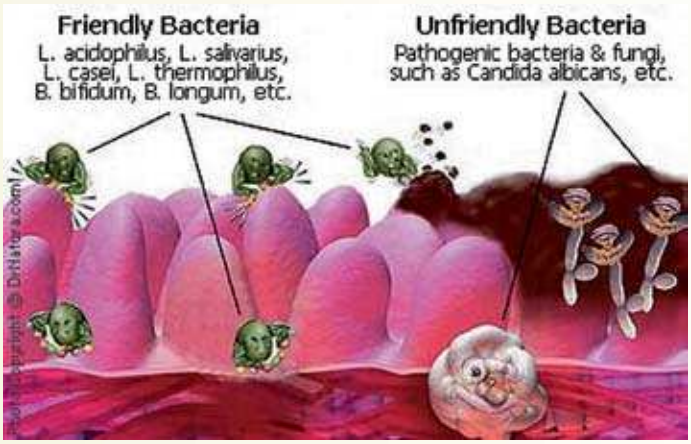
The first ever commercially available and claimed probiotic product was Yakult – a dairy product made by fermenting a mixture of skimmed milk with a special strain of the bacterium *Lactobacillus casei* Shirota. It was created by a Japanese scientist Minoru Shirota who made

this nutraceutical preparation of fermented milk and started selling it as a health booster drink.

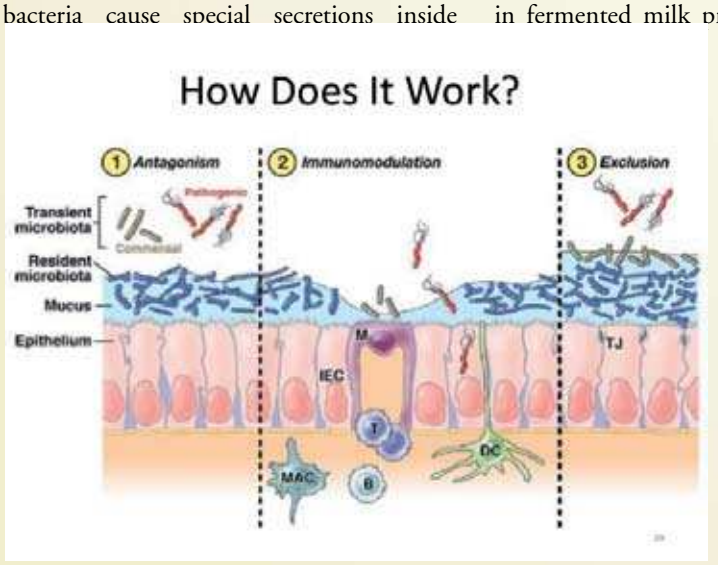
How probiotics work

Probiotics assist in maintaining balance in between the good and bad organisms within the digestive tract. Upon consumption the probiotic organisms tend to adhere tightly to the mucus membrane of intestine. After adhesion, they rapidly multiply and form colonies.

There are a number of studies conducted to understand the possible mode of action of probiotics in the intestinal gut. The activities of the probiotics in the intestinal gut lead to competitive exclusion of pathogens, production of bacteriocins (proteinaceous toxins produced by bacteria to inhibit the growth of similar or closely related bacterial strain), production of organic acids and altered absorption of the intestinal mucus membrane. It was observed that probiotic bacteria cause special secretions inside the gut. These secretions contain certain chemicals having antibacterial, antiviral and antifungal characteristics, thereby resisting the pathogens. It was also found that probiotic microorganisms enhance barrier integrity of intestinal mucus membrane and prevent entry of pathogens and their metabolites inside the intestinal walls. Not only these, certain probiotics reduce intestinal pH leading to increase in acidity. Acidic environment is helpful in absorption of essential nutrients such as iron in the digestive tract. Probiotics also provide suitable environment for better absorption of nutrients.



Friendly and unfriendly bacteria



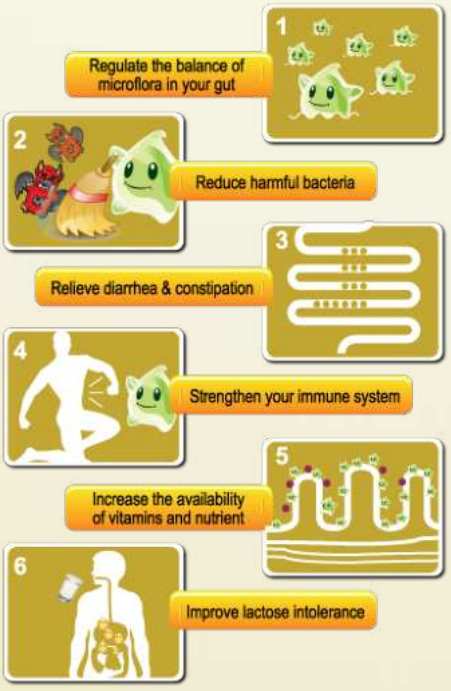
How probiotics work

Health benefits of probiotics

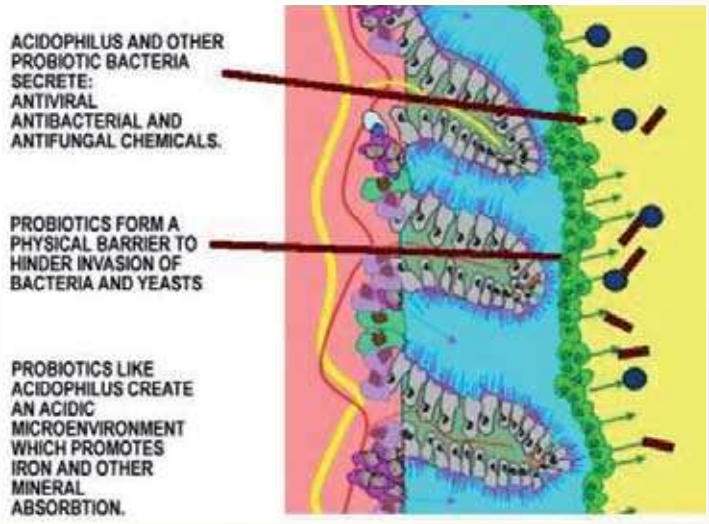
Several studies have been conducted on animals and humans to learn about the effect of probiotics. In 1907, Metchnikoff proposed that the acid-producing bacteria in fermented milk products could prevent "fouling" in the large intestine and, if consumed regularly, lead to a longer, healthier life. The first clinical trial was performed in the 1930s on the effect of probiotics on constipation. In 1983, S.H. Kim and S.E. Gilliland found that probiotic bacteria containing β-galactosidase can be added to food to improve lactose digestion. In 1994, the World Health Organization deemed probiotics to be the next-most important immune defence system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. Probiotics were also found to effectively control serum cholesterol levels in adult human experiments.

The effects of probiotic and conventional yoghurt on the plasma lipid profile of women having a normal amount of cholesterol in the blood were also studied. It was found that regular consumption of both probiotic and conventional yoghurt for four weeks had a positive effect on the lipid profile assessed by the total/HDL and LDL/HDL-cholesterol ratios in plasma of healthy women. In another study, significant reduction in the total cholesterol, triglycerides, LDL and VLDL-cholesterol and increased HDL-cholesterol levels was observed in rats fed with *dahi* containing probiotic *Lactobacillus acidophilus* and *Lactobacillus casei*. The antimicrobial activities of probiotics from commercially available probiotic drink was studied which proved the presence of antimicrobial activity among the products.

While taking antibiotics frequently or for a long period of time, useful microorganisms of the intestine get destroyed along with the pathogens. In this situation, antibiotic-associated diarrhoea (AAD) results from an imbalance in the colonic microbiota (community of microbes that reside in the body). Alteration of microbiota changes carbohydrate metabolism with decreased short-chain fatty acid absorption and osmotic diarrhoea as a result. Another consequence of antibiotic therapy leading to diarrhoea is overgrowth



Modes of action of probiotics inside the gut



Benefits of probiotics

of potentially pathogenic organisms such as *Clostridium difficile*. Research has showed that probiotic treatment might reduce the incidence and severity of AAD. Carefully selected probiotic strains may be useful in the treatment of acute diarrhoea, and also possibly in rotavirus infections in children and travellers' diarrhoea in adults. Probiotic strain *Bifidobacterium animalis* showed a reduction in discomfort and bloating in individuals with constipation-predominant Irritable Bowel Syndrome (IBS) as well.

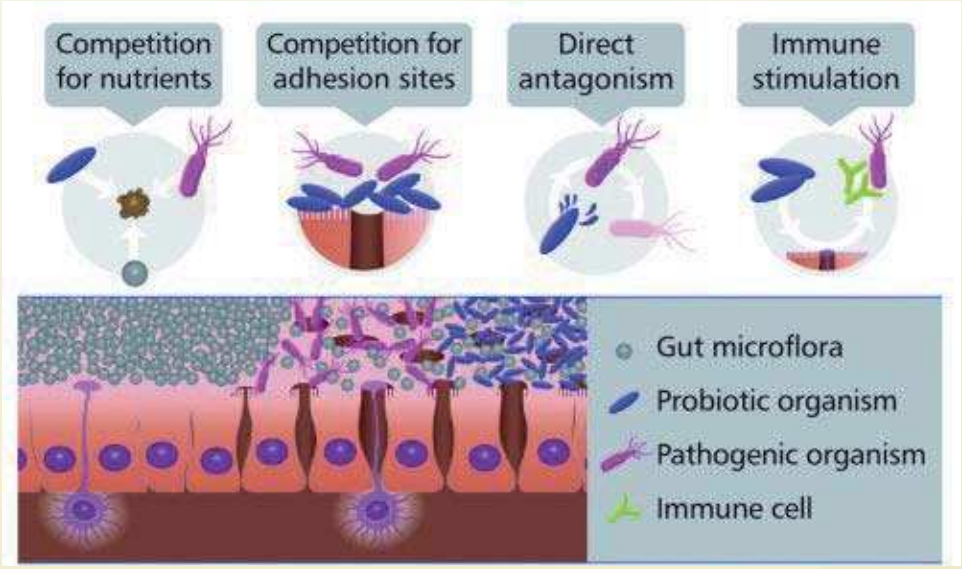
During the process of digestion and metabolism, some carcinogenic compounds may be produced in digestive tract. Some strains of LAB (*Lactobacillus delbrueckii* subsp. *bulgaricus*) have demonstrated anti-mutagenic effects thought to be due to their ability to bind with such carcinogenic compounds. It was also observed that some probiotic strains exert anti-carcinogenic effects by decreasing the activity of an enzyme called β–glucuronidase, which is believed to produce carcinogens in the digestive system. Probiotics in this context are beneficial in preventing colon cancer.

Probiotics may affect pathogens by means of competitive inhibition (i.e., by competing for growth) and there is evidence to suggest that they may improve immune function by increasing the number of IgA-producing plasma cells, increasing or improving phagocytosis (an important defence against infection) as well as increasing the proportion of T lymphocytes and natural killer cells. All these cells are important soldiers of our immune system and this way probiotics may help boosting immune system and disease fighting ability of our body.

Criteria for selection of microorganisms as probiotics

Any microorganism cannot be termed as probiotic. There are specific characteristics that define probiotic microorganisms. If a microorganism or its strains possess these characteristics they can be claimed as probiotics. Probiotics should be non-pathogenic and non-toxic. They must not be hydrolysed nor absorbed in the upper gastrointestinal tract. Further, they should be able to

- Exert a beneficial effect on the host
- Utilise the nutrients and substrates in a normal diet
- Remain viable throughout the shelf-life of the product
- Withstand transit through the GI tract
- Survive the passage through the digestive system
- Attach to the intestinal epithelia and colonise
- Able to produce antimicrobial substances against pathogens
- Able to stabilise the intestinal microflora and be associated with health benefits.



Mechanism of action of probiotics

Probiotic products of Indian market

Many national and multinational companies are selling many products as probiotic food items. In Indian market, leading co-operative federation like Amul has launched a variety of products with probiotic properties. Probiotic products such as curd, buttermilk, fermented milk, yoghurt, *lassi*, ice cream, etc., are becoming popular amongst the consumers.

While purchasing probiotic product it is very essential to read the expiry date of the product carefully. As probiotic organisms have limited and specific life period, consumption of expiry dated product would not provide sufficient number of live probiotic microorganisms. In such case, one may not get the actual health benefits of probiotics. Storage temperature of the products is also a very important factor to be considered before purchase of the product. Fluctuation in temperature may adversely affect the viable counts of probiotic organisms. Probiotic product should be stored at refrigerated temperature and should be consumed fresh. So, next time whenever you plan to purchase dairy products, go for beneficial probiotic products and be delighted with the good taste along with good health!

Dr. Preeti H. Dave is Assistant Professor of Food Science & Nutrition at S.D. Agricultural University, S.K. Nagar- 385506, Distt. Banaskantha, Gujarat.

Nanotechnology in Environmental Remediation

Ashutosh Mohanty
E-mail: rtr.ashutosh@yahoo.com

Materials science has become a versatile field of science and technology with multifarious applications. Many of the new materials are endowed with unique properties such as optical, photo catalytic, catalytic, dielectric, antimicrobial, mechanical, and electrical, which make them useful for applications in electronics, medical, agricultural, mechanical, environmental, and many other important fields. Nanomaterials are part of these new-age materials.

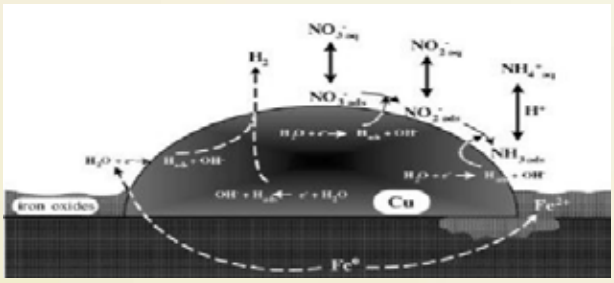
One of the most socially relevant aspects of nanomaterials is in the field of environmental remediation. Diverse applications of nanomaterials in decontamination of air, water and soil have been successfully demonstrated in the recent past. The availability of large surface area and structural defects in these materials are responsible for these properties and play a crucial role in the use of nanomaterials in environmental remediation by removing various pollutants. One of the early applications of such materials has been in the decomposition of halogenated carbon compounds and pesticide removal. In ancient times people used carbon material, namely charcoal and other porous materials for water purification. Activated charcoal is widely used in water purification. Advanced techniques are also being used for the preparation of thin membranes and ion-exchange materials, namely zeolites for waste water treatment and for the removal of contaminants from water. Some of the other materials used for water purification are described below.

Graphene-sand composite (Nanoclays)

Graphene is a fascinating member of the carbon family. It has a structural similarity with graphite, but unlike in graphite it has no layered structure but only a single layer of hexagonally arranged carbon atoms (planar structure). Chemically synthesised graphene and graphene oxide can be anchored on the surface of river sand (silica; SiO_2) to make effective adsorbents to remove heavy metals, pesticides as well as other organic effluents.

This material shows an outstanding activity compared to that of conventional charcoal or activated charcoal. There have been many approaches to attach graphene on sand surfaces with the help of suitable binder such as chitosan – a sugar obtained from the hard outer skeleton of shellfish, including crab, lobster, and shrimp.

Carbon for graphene is obtained from natural sugar through dehydration. Carbon so obtained can be anchored on inorganic surfaces like silica or any other matrix and some chemical transformations can be done to obtain carbon in the form of graphene which is a highly effective adsorbent. Tests using graphene-sand composite have shown that it can degrade and decolourise dyes like rhodamine 6G, pesticides like chloropyrifos, and also some coloured soft drinks. .



Bimetallic nanoparticles

Bimetallic nanoparticles have been found to be very effective for the destruction of halogenated organic compounds, especially pesticides. In past few years, zero-valent iron has een found to be a good degrader of pesticides containing chlorine such as DDT, Aldrin, Dieldrin, Endosulfan, etc. But this granular form of iron has a serious limitation due to its low reactivity. For example, reduction of tetrachloroethene (also known industrially as perchloroethylene, PERC or PCE) and trichloroethene (TCE) by zero-valent iron has been observed to produce toxic byproducts like cis-1, 2-dichloromethane (DCM) and vinyl chloride (VC) and not remove the chlorine completely. The low reactivity of iron is probably due to the formation of passive layer of hydroxides, carbonates, nitrates on the surface.

Currently, nanoparticles of some other metals are being used, especially zinc, tin, palladium, etc., for the degrading halogenated organic compounds quickly and efficiently. In a recent study it has been revealed the palladised iron can completely remove chlorine from many chlorinated organic compounds. This enhanced activity of this material is due the catalytic behaviour of palladium. In the same way nickel-iron composite (Ni/Fe) has been made and proved to be a marvellous dehalogenation agent due to the enhanced catalytic behaviour of nickel. This metallic catalyst prevents the formation of the toxic byproducts by dehalogenation of chlorinated pesticides.

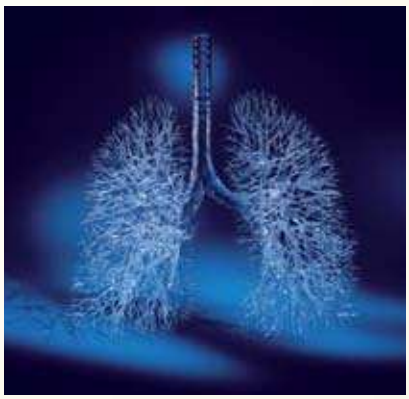
One major problem with surface and ground waters is the contamination by nitrate ion. To rectify this particular problem environmental chemists are using bimetallic nanomaterials, especially surface catalysed iron. Below pH of 4 this material has been proved to be a very good degrader of nitrates.

Continued on page 19

Interstitial lung disease
When the lung substance gets scarred

Dr. Yatish Agarwal
E-mail: dryatish@yahoo.com

Breathing day in and day out, the lungs take in the life-giving oxygen and exhale carbon dioxide. This business of air exchange takes place within the lungs' tiny air sacs called the alveoli. The alveoli, in turn, are supported by a lace-like network of tissue called the interstitium. The interstitium also carries the tiny blood vessels, which pick up the oxygen from the air in the lungs and carry it to different parts of the body through the circulating blood.



In some people, due to a variety of reasons, the interstitium suffers damage and gets thickened. This interrupts the easy flow of oxygen and carbon dioxide between the alveoli and circulating blood and produces shortness of breath. Since the interstitium is the seat of disease, the malady is called interstitial lung disease.

An umbrella term used for a large group of lung maladies, interstitial lung disease is a difficult condition to treat. While it causes a progressive scarring of the supportive tissue in the lungs, it eventually affects a person's ability to breathe and get enough oxygen into the bloodstream.

Interstitial lung disease — often referred to by the acronym ILD — can be caused by long-term exposure to hazardous materials, such as asbestos. Some types of autoimmune diseases, such as rheumatoid arthritis, also can cause interstitial lung disease. In most cases, however, the causes remain unknown.

Some forms of interstitial lung disease are short-lived; others are chronic and irreversible. However, once lung scarring occurs, it is generally permanent. Medications may slow the damage of interstitial lung disease, but many people never regain full use of their lungs. Lung transplant is an option for some people who have interstitial lung disease.

What causes interstitial lung disease?

Interstitial lung disease seems to occur when an injury to the lungs triggers an abnormal healing response. Ordinarily, a person's body generates just the right amount of tissue to repair damage. But in interstitial lung disease, the repair process goes awry and the tissue around the air sacs (alveoli) becomes scarred and thickened. This makes it more difficult for oxygen to pass into the bloodstream. The primary signs and symptoms of interstitial lung disease relate to this change, and include shortness of breath at rest or aggravated by exertion, and dry cough.

Types of interstitial lung disease

The list of conditions and substances that can lead to interstitial lung disease is long. Even so, in most cases, the causes are never found. Disorders without a known cause are grouped together under the label of idiopathic interstitial pneumonias, the most common and deadly of which is idiopathic pulmonary fibrosis.

A variety of conditions can produce thickening of the interstitium and lead to interstitial lung disease. The thickening can be due to inflammation, scarring, or extra fluid (oedema). The more common types of interstitial lung disease include:

Interstitial pneumonia

Bacteria, viruses, or fungi may infect the interstitium of the lung. A bacterium called *Mycoplasma pneumonia* is the most common cause.

Idiopathic pulmonary fibrosis

A chronic, progressive form of fibrosis (scarring) of the interstitium. Its cause is unknown.

Nonspecific interstitial pneumonitis

Interstitial lung disease that's often present with autoimmune conditions such as rheumatoid arthritis or scleroderma.

Hypersensitivity pneumonitis

Interstitial lung disease caused by ongoing inhalation of dust, mould, or other irritants.

Cryptogenic organising pneumonia (COP)

A pneumonia-like interstitial lung disease but without any infection. COP is also called bronchiolitis obliterans with organising pneumonia (BOOP).

Acute interstitial pneumonitis

A sudden, severe interstitial lung disease, often requiring life support.

Desquamative interstitial pneumonitis

An interstitial lung disease that's partially caused by smoking.

Sarcoidosis

A condition causing interstitial lung disease along with swollen lymph nodes, and sometimes heart, skin, nerve, or eye involvement.

Asbestosis

Interstitial lung disease caused by asbestos exposure.

Variety of triggers

A number of factors may make a person more susceptible to develop interstitial lung disease. These include:

Age

Although infants and children may sometimes develop the disorder, interstitial lung disease is much more likely to affect adults.

Gastro esophageal reflux disease

If a person has uncontrolled acid reflux or indigestion, s/he may be at increased risk of interstitial lung disease.

Smoking
Some forms of interstitial lung disease are more likely to occur in people with a history of smoking, and active smoking may make the condition worse, especially if there is associated emphysema.

Oxygen
Continually inhaling very high levels of oxygen can harm the lungs.

Exposure to occupational and environmental toxins
If a person works in mining, farming or construction or for any reason is exposed to pollutants known to damage lungs, the risk of interstitial lung disease is increased.

Long-term exposure to a number of occupational and environmental toxins and pollutants, including silica dust, asbestos fibres, grain dust, bird and animal droppings, and indoor hot tubs can damage the lungs.

Medical conditions
Systemic lupus erythematosus, rheumatoid arthritis, scleroderma and sarcoidosis can also result in lung damage and produce interstitial lung disease.

Medications
Many drugs can damage your lungs, especially:

Anti-cancer drugs: Drugs designed to kill cancer cells, such as methotrexate and cyclophosphamide, can also damage lung tissue.

Heart medications: Some drugs used to treat irregular heartbeats, such as amiodarone or propranolol, may harm lung tissue.

Antibiotics: Some antibiotics, like Nitrofurantoin and Sulfasalazine can cause lung damage.

Radiation treatment
Some people who receive radiation therapy for lung or breast cancer show signs of lung damage months or sometimes years after the initial treatment. The severity of the damage depends on how much of the lung was exposed to radiation, the amount of radiation received, the presence of underlying lung disease, and whether chemotherapy also was used

Complications
Interstitial lung disease can lead to a series of life-threatening complications, including:

High blood pressure in the lungs (pulmonary hypertension)
Unlike systemic high blood pressure, this condition affects only the arteries in the lungs. It begins when scar tissue or low oxygen levels restrict the smallest blood vessels, limiting blood flow in the lungs. This in turn raises pressure within the pulmonary arteries. Pulmonary hypertension is a serious illness that becomes progressively worse.

Right-sided heart failure (cor pulmonale)
This serious condition occurs when the heart's lower right chamber (right ventricle) — which is less muscular than the left — has to pump harder than usual to move blood through obstructed pulmonary arteries. Eventually the right ventricle fails from the extra strain. This is often a consequence of pulmonary hypertension.

Respiratory failure


In the end stage of chronic interstitial lung disease, respiratory failure occurs when severely low blood oxygen levels along with rising pressures in the pulmonary arteries and the right ventricle cause heart failure.

Recognising the symptoms
The most common symptom of all forms of interstitial lung disease is shortness of breath. Nearly all people with interstitial lung disease will experience breathlessness, which may get worse over time.

Other symptoms of interstitial lung disease include:

- Cough, which is usually dry and nonproductive.
- Weight loss, most often in people with COP or BOOP.

In most forms of interstitial lung disease, the shortness of breath develops slowly, usually over months. In interstitial pneumonias or acute interstitial pneumonitis, however, symptoms come on more rapidly in hours or days.

Seeing a doctor
By the time symptoms appear, irreversible lung damage has often already occurred. Nevertheless, it's important to see a doctor at the first sign of breathing problems. Getting an early and accurate diagnosis is important for proper treatment.

Often, a person would first bring his symptoms to the attention of a family doctor. S/he may refer you to a pulmonologist — a doctor who specialises in lung disorders. The specialist might advice you to undergo a variety of tests — blood work, chest X-ray, a CT scan of the chest and pulmonary function testing.

Tests and scans
Identifying and determining the cause of interstitial lung disease can be extremely challenging. Firstly, an unusually large number of disorders fall into this broad category. Secondly, the signs and symptoms of a wide range of medical conditions can mimic interstitial lung disease, and doctors must rule these out before making a definitive diagnosis.

The following tests may come in useful:

Pulmonary function tests


Oximetry : This simple test uses a small device placed on one of your fingers to measure the oxygen saturation in your blood. Oximetry can serve as an easy way to monitor the course of the disease, sometimes more accurately than a chest X-ray can.

Spirometry and diffusion capacity: This test requires you to exhale quickly and forcefully through a tube connected to a machine that measures how much air your lungs can hold, and how quickly you can move air out of your lungs. It also measures how easily oxygen can move from the lungs into the bloodstream.

Imaging tests
Chest X-ray: The lung damage associated with many types of interstitial lung disease often shows up in characteristic patterns on chest X-rays. Chest X-rays may also be used to track the progression of disease.

If your family physician had a chest X-ray done as part of your initial evaluation, bring that with you when you see a pulmonologist. It will help the pulmonologist make a diagnosis if he or she can compare an old chest X-ray with the results of a current X-ray. The actual X-ray image is more important to your doctor than is the report alone.

Computerised tomography (CT) scan chest: CT scanners use a computer to combine X-ray images taken from many different angles to produce cross-sectional images of internal structures. A high-resolution CT scan can be particularly helpful in determining the extent of lung damage caused by interstitial lung disease. It can show details of the fibrosis, which can be helpful in narrowing down the diagnosis.

Echocardiogram : A sonogram for the heart, an echocardiogram uses sound waves to visualise the heart. It can produce still images of your heart's structures, as well as videos that show how your heart is functioning. This test can evaluate the amount of pressure occurring in the right side of your heart.

Lung tissue analysis

Often, pulmonary fibrosis can be definitively diagnosed only by examining a small amount of lung tissue (biopsy) in a laboratory. The tissue sample may be obtained in one of these ways:

Bronchoscopy : In this procedure, your doctor removes very small tissue samples — generally no larger than the head of a pin — using a small, flexible tube (bronchoscope) that's passed through your mouth or nose into your lungs. The risks of bronchoscopy are generally minor — most often a temporary sore throat and hoarseness from the bronchoscope — but the tissue samples are sometimes too small for an accurate diagnosis.

Bronchoalveolar lavage : In this procedure, your doctor injects about a tablespoon of salt water through a bronchoscope into a section of your lung, and then immediately suctions it out. The solution that's withdrawn contains cells from your air sacs. Although bronchoalveolar lavage samples a larger area of the lung than other procedures do, it may not provide enough information to diagnose pulmonary fibrosis.

Surgical biopsy : Although this is a more invasive procedure with potential complications, it's often the only way to obtain a large enough tissue sample to make an accurate diagnosis. During the procedure under general anesthesia, surgical instruments and a small camera are inserted through two or three small incisions between your ribs. The camera allows your surgeon to view your lungs on a video monitor while removing tissue samples from your lungs.

What you can do

Being actively involved in your own treatment and staying as healthy as possible are essential to living with interstitial lung disease. For that reason, it's important to:

Stop smoking : If you have lung disease, the best thing you can do for yourself is to stop smoking. Talk to your doctor about options for quitting, including smoking cessation programs, which use a variety of proven techniques to help people quit. As secondhand smoke can also be harmful to your lungs, don't allow other people to smoke around you.

Eat well: People with lung disease may lose weight both because it's uncomfortable to eat and because of the extra energy it takes to breathe. These people need a nutritionally rich diet that contains adequate calories. A dietitian can give you further guidelines for healthy eating.

Get vaccinated: Respiratory infections can worsen symptoms of interstitial lung disease. Make sure you receive the pneumonia vaccine and an annual flu shot.

Coping well : Living with a chronic lung disease is emotionally and physically challenging. Your daily routines and activities may need to be adjusted, sometimes radically, as breathing problems worsen or health care needs take priority in your life. Feelings of fear, anger and sadness are normal as you grieve for the loss of your old life and worry about what's next for you and your family.

Share your feelings with your loved ones and your doctor. Talking openly may help you and your loved ones cope with the emotional challenges of your disease.

Medical treatments

Some treatments may improve symptoms temporarily or slow the disease's progress. Others help improve quality of life. Your doctor may try out the following treatments with varying results:

Medications

Corticosteroids: In some forms of interstitial lung disease, ongoing inflammation in the lungs causes damage and scarring. Corticosteroids like prednisone and methylprednisolone reduce the activity of the immune system. This reduces the amount of inflammation in the lungs and the rest of the body.

N-acetylcysteine: This potent antioxidant may slow the decline of lung function in some forms of interstitial lung disease. It does not improve people's survival from interstitial lung disease, however.

Azathioprine: This drug suppresses the immune system. It has never been proven to improve interstitial lung disease, but some studies suggest it might help.

Oxygen therapy

You may benefit with round-the-clock oxygen treatment. Using oxygen can't stop lung damage, but it can:

- Make breathing and exercise easier
- Prevent or lessen complications from low blood oxygen levels
- Reduce blood pressure in the right side of your heart
- Improve your sleep and sense of well-being

Pulmonary rehabilitation

The aim of pulmonary rehabilitation is not only to improve daily functioning but also to help people with interstitial lung disease live full, satisfying lives. To that end, pulmonary rehabilitation programs focus on:

- Physical exercise, to improve your endurance
- Breathing techniques that improve lung efficiency
- Emotional support
- Nutritional counseling

Surgery

In advanced interstitial lung disease causing severe impairment, a lung transplant may be the best option. Most people undergoing lung transplant for interstitial lung disease make large gains in quality of life and their ability to exercise.

Prof Yatish Agarwal is a physician and teacher at New Delhi's Safdarjung Hospital. He has authored 47 popular health-books.

Recent Developments in Science and Technology

Biman Basu
E-mail: bimanbasu@gmail.com

Potentially habitable Earth-like planets discovered

Amidst the increasing tempo of search for Earth-like planets around distant stars, an international team of astronomers from the Massachusetts Institute of Technology in USA, the University of Liège in Belgium, and elsewhere, have reported discovery of three planets orbiting a white dwarf star, located in the constellation of Aquarius, about 39 light-years from Earth. According to the astronomers, the newly discovered planets have sizes and temperatures similar to those of Venus and Earth and could be the best targets found so far for the search for life outside the Solar System. The team used the robotic 0.6-metre telescope at European Southern Observatory's La Silla Observatory in Chile known as TRAPPIST (TRAnsiting Planets and PlanetIsimals Small Telescope) looking for ultra-cool dwarfs – stars far cooler and dimmer than the Sun. The white dwarf star has been named TRAPPIST-1 (*Nature*, 2 May 2016 | DOI: 10.1038/nature17448).

An artist's impression of the star TRAPPIST-1, as seen from above one of the newly-discovered exoplanets. (Credit: ESO/M. Kornmesser)

During observations of the brown dwarf, the team of astronomers led by Michaël Gillon, of the Institut d'Astrophysique et Géophysique at the University of Liège in Belgium, found that this dim and cool star faded slightly at regular intervals, indicating that several objects were passing between the star and the Earth. Detailed analysis showed that the dimming was caused by three planets with similar sizes to the Earth, orbiting the star.

Further observations with larger telescopes, including the HAWK-I instrument on ESO's 8-metre Very Large Telescope in Chile, have shown that the planets orbiting TRAPPIST-1 have sizes very similar to that of Earth. Two of the planets have orbital periods of about 1.5 days and 2.4 days respectively, and the third planet has a range 4.5 to 73 days. According to the astronomers, "With such short orbital periods, the planets are between 20 and 100 times closer to their star than the Earth is to the Sun. The structure of this planetary system is much more similar in scale to the system of Jupiter's moons than to that of the Solar System".

According to the astronomers, despite the fact that the three planets orbit very close to their host dwarf star, they are not very hot – the inner two planets may be receiving about four times and twice, respectively, the amount of radiation received by the Earth, because their star is much fainter than the Sun. Although that still makes them too hot to support life as we know on Earth, the astronomers feel it may be still possible that they possess habitable regions on their surfaces. The third an outer planet's orbit is not yet well known; it probably receives less radiation than the Earth does from the Sun, but maybe still be lying within the habitable zone.

Astronomers usually search for signs of life on distant planets by studying the effect that the atmosphere of a transiting planet has on the light from the star reaching Earth. But, for planets orbiting most stars this tiny effect is extremely difficult to detect because any slight variation in light is swamped by the brilliance of the background starlight. However, it may be easier for astronomers to look for signs of life on the newly discovered planets because the variations are expected to be big enough to be detected against the background of a dim white dwarf like TRAPPIST-1.

This discovery has certainly opened up a new direction in our search for extra-terrestrial life, as around 15% of the stars near to the Sun are known to be ultra-cool dwarf stars. It also serves to highlight that the search for exoplanets has now entered the realm of potentially habitable cousins of the Earth. The TRAPPIST survey is a prototype for a more ambitious project called SPECULOOS that will be installed at ESO's Paranal Observatory in Chile.

Replica of Martian surface found in Gujarat

A replica or "terrestrial analogue" of the Martian surface has been discovered in Gujarat by a team of Indian scientists from the Space Applications Centre (SAC-ISRO), Ahmedabad, Indian Institute of Technology-Kharagpur, and the National Geophysical Research Institute (NGRI), Hyderabad. This work is part of a programme initiated by SAC-ISRO under its Mars mission. The team reported the finding on the basis of identification of the presence of a rare mineral called 'jarosite' through spectroscopic studies in a place known as Matanumadh (86 km northwest of Bhuj) in Kachch district of Gujarat. Presence of the rare mineral was reported from various parts of the surface of the Red Planet by NASA's Mars exploration rover *Opportunity* in 2004. Since then, other rovers have detected jarosite at several locations on the planet's surface (*Journal of Geophysical Research: Planets*, March 2016, DOI: 10.1002/2015JE004949).

The sulphate mineral jarosite is considered a key indicator of hydrous, acidic, and oxidising conditions on the surface of early Mars. The researchers argue that the overall geological setting of the Matanumadh area, with this unusual mineral assemblage, mimics the geological environment of many of the identified jarosite localities on Mars and can be considered "as a Martian analogue from this perspective". In fact, the researchers say, as a clone, the Indian site more closely

The landscape of Matanumadh mimics the geological environment of many of the identified jarosite localities on Mars.

resembles the Martian surface than known Western Australian jarosite localities.

According to the scientists, the significance of the discovery is multi-fold and could have implications in the way we explore the Martian surface. "The two essential conditions for jarosite formation are near-surface acidic water and oxidising conditions. Understanding how jarosite formed in the Matanumadh Formation may shed light on the final stages of aqueous (water-based) activity in parts of the Martian surface", says Souvik Mitra of IIT-Kharagpur and a member of the team. According to Saibal Gupta, Professor, Department of Geology and Geophysics at IIT-Kharagpur and another member of the team, "Rather than sending up sophisticated robots and probes to Mars to study it, investigations could now be carried out right at the Matanumadh Formation at a much reduced cost, to understand the events that may have occurred on Mars a few billion years ago".

Of course, there can be no substitute for human exploration of the Martian surface, but that could be quite some time in the future. Till then, these analogue localities could provide a starting point for knowing what to expect. In fact, this work is a demonstration of what collaboration between scientists from different organisations within India can do.

Microbots to clean up polluted water

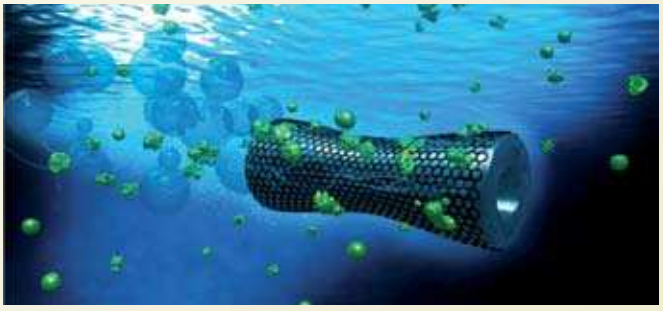
Water pollution is a growing problem around the world. The planet's oceans are increasingly becoming the sites of enormous amounts of human-generated waste, with estimates putting the amount of plastic now in our oceans close to 8 million tonnes. Heavy metal pollution in water is a common problem stemming from industrial activities, including the manufacturing of batteries and electronics, as well as mining and electroplating. These activities produce water contaminated with heavy metals like lead, mercury, cadmium, chromium and arsenic the safe disposal of which is an ever-present problem. Currently most of this polluted water is discharged into water bodies which pose a safety hazard to living organisms and the environment.

Currently, new research in nanotechnology is developing new nanosystems and nanomaterials for the fast and efficient removal of pollutants and heavy metals from water. Researchers from the Institute for Intelligent Systems in Germany and the Institute for Bioengineering of Catalonia in Spain have now come up with a novel solution of the problem – to use minute microbots (miniature robots) to help remove toxic material from industrial wastewater. A new study shows that a swarm of hundreds of thousands of tiny microbots, each smaller than the width of a human hair, can be deployed into industrial wastewater to absorb and remove toxic heavy metals (*Nano Letters*, 21 March, 2016 | DOI: 10.1021/acs.nanolett.6b00768).

The current study was focussed specifically on removing lead from wastewater using tube-shaped microbots with three functional layers. The outer layer of graphene oxide adsorbs the lead from the water. The middle layer made up of nickel atoms makes the microbots ferromagnetic that allows a person to remotely control where the microbots swim, by using an external magnetic field. The inner layer of platinum atoms gives the microbots the ability to self-propel themselves through water. When hydrogen peroxide is added to the wastewater, the platinum decomposes the hydrogen peroxide into water and oxygen microbubbles, and ejecting the microbubbles from the back of the microbot propels it forward.

The microbots are self-propelled systems designed for the capture, transfer, and removal of a heavy metal (e.g., lead) and its subsequent recovery for recycling purposes. According to the researchers, mobile graphene oxide-microbots remove lead rapidly, cleaning water from 1,000 ppb (parts per billion) level down to below 50 ppb in 60 min. When the microbots are finished adsorbing the lead, a magnetic field can be used to collect them all from the water. Then the microbots are treated in an acidic solution to remove the lead ions, which can later be recovered and reused. The same microbots can then be reused for further lead clean-up, potentially offering a more effective and economical way to remove heavy metals than previous methods.

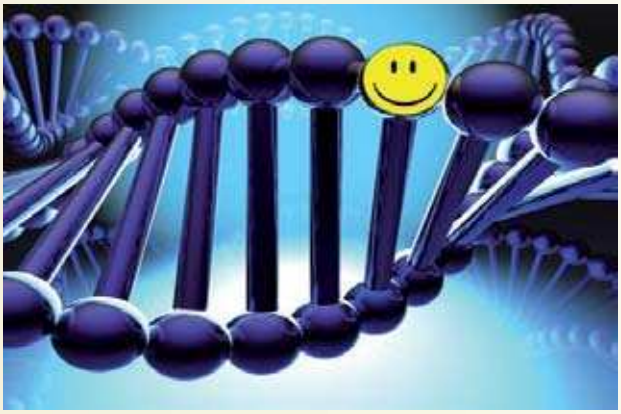
At the moment, the microbots only work for lead, but the team plans to extend the use of microbots to other contaminants and work on a way to mass-produce the robots at a low cost. According to Samuel Sánchez of Max-Planck Institute for Intelligent Systems, Stuttgart, Germany and member of the team, "This work is a step toward the development of smart remediation system where we can target and remove traces of pollutant without producing an additional contamination,"



An illustration of a self-propelled "microbot" that could be used to capture, transfer and remove heavy metals from water.

Gene for happiness discovered

Happiness and wellbeing are the topics of an increasing number of scientific studies in a variety of academic disciplines, especially in view of the growing body of evidence suggesting that wellbeing is a factor in mental and physical health. It has long been a mystery why some people always seem to be happy while some always seem to suffer from depression. Now scientists seem to have found the answer. For the first time in history, researchers have identified the parts of the human genome that could



For the first time researchers have identified the parts of the human genome that could explain the differences in how humans experience happiness.

explain the differences in how humans experience happiness. The genetic variants for happiness are mainly expressed in the central nervous system, the adrenal glands and the pancreatic system. The researchers have also found a genetic overlap between happiness and depression.

These are the findings of a large-scale international study with more than 3,00,000 people carried out by a team led by Meike Bartels and Philipp Koellinger from Vrije Universiteit in the Netherlands, and Daniel Benjamin from the University of Southern California, Los Angeles, USA (*Nature Genetics*, 18 April 2016 | doi:10.1038/ng.3552). This research is said to be the largest ever study into the genetic variants for happiness. It was successfully completed thanks to the assistance of 181 researchers from 145 scientific institutes, including medical centres in Rotterdam, Groningen, Leiden and Utrecht, and the universities of Rotterdam and Groningen.

The researchers have identified three genetic variants associated with subjective wellbeing (happiness), two variants associated with depressive symptoms, and also eleven variants associated with neuroticism (a fundamental personality trait characterised by anxiety, fear, moodiness, worry, envy, frustration, jealousy, and loneliness). Before this study, research on twins and families using information from the Netherlands Twin Register and other sources had shown that individual differences in happiness and wellbeing can be partially ascribed to genetic differences between people. But no substantive evidence was available.

Professors Bartels and Koellinger, in collaboration with scientists in 17 countries, studied the phenotypes (the appearance of an organism as a consequence of the interaction of its genes and the environment) in the DNA of more than 3,00,000 people. Then they asked the participants to discuss how happy they feel about their life, if they have ever had depression or depressive symptoms and signs of neurotic behaviour. They also looked into physical traits that can have an impact on mood, including smoking and body mass index. Analysis of the data revealed that subjective wellbeing, depression and neuroticism are influenced by the same set of genes expressed in the central nervous system, adrenal glands and pancreatic system.

The particular DNA in question, called the FAAH gene, encodes a protein that is responsible for the hydrolysis of a number of primary and secondary fatty acid amides and affects feelings of pleasure and pain. According to the scientists, people with a particular version of this gene tend to be more cheerful individuals. However, wealth and health were found to have little effect on happiness.

Biman Basu is a former editor of the popular science monthly Science Reporter, published by CSIR, He is a winner of the 1994 'NCSTC National Award for Science Popularisation'. He is the author of more than 45 popular science books.

Nanotechnology in Environmental Remediation *(Continued from page 25)*

Another synthetic bimetallic nanoparticle is Pd/Au, which can reduce the chlorinated compounds from surface and ground water. Some researchers synthesised Pd-supported on gold nanoparticles and found that these catalysts were considerably more active than palladium nanoparticles. Fe-Pd bimetallic nanoparticles, with 0.2% w/w of sodium carboxymethyl cellulose (CMC) as stabiliser, have been found effective in degrading the chlorinated herbicides lindane and atrazine.

Conclusion

The use of nanomaterials in detection and removal of pollutants provides greater sensitivity, lower cost, shorter time, in-line and real-time detection, and portability in environmental remediation. In addition, metal and metal oxide nanomaterials can be used to remove organic pollutants and metals. This method is effective and promising, and can be used in improving the quality of water and air. Nano-membranes made up with carbon-based materials have found applications in the production of potable water, water reclamation, removal of metals, dyes, and removal of pesticides from the contaminated water. Further improvements in application of environmental remediation are necessary for better selectivity in the removal of materials, resistance to changes in pH and concentrations of chemicals present in the contaminated water, stability for longer time, and cost optimisation.

Ashutosh Mohanty is M.Sc. (1st Year) student in Department of Geology, Utkal University, Bhubaneswar, Odisha.