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Editorial

Fluorescence spectroscopy in is numerous variations has become a most powerful bioanalytical and diagnostic tool in terms of versatility. Recent advances in the development of fluorescent biosensors have made an outstanding contribution to elucidating not only the roles of individual biomolecules, but also the dynamic intracellular relationships between these molecules.

Gravitational waves are ripples in the curvature of spacetime that propagate as waves, generated in certain gravitational interactions and travelling outward from their source. Predicted in 1916 by Albert Einstein on the basis of his theory of general relativity, gravitational waves transport energy as gravitational radiation, a form of radiant energy similar to electromagnetic radiation. You can see the glimps of a Gravitational waves history to till the date research and prediction

Nowadays science is that much develop that's shows using light we can control protein transport from cell nucleus. The researchers are convinced that their new optogenetic tool can also be used to make important discoveries on the dynamics of protein transport and its influence on cell behaviour . The development of innovative molecular tools is therefore the key to understanding basic cellular functions as well as the mechanisms that cause illness.

The authors reviews the complications during the NSNephrotic syndrome are mortal infections, thrombosis, and edema due to significant protein loss. Currently, the etiologies of NS have been revealed due to various acquired as well as genetic defects and its progressive forms can lead to chronic and end-stage renal disease. Even authors point out that formation of metal complexes results into wide variety of coordination spheres, oxidation states and redox potential will alter the kinetic and thermodynamic properties of the complexes towards biological receptors. The present review describes the importance of some metal ions and metal based drugs having promising results in the treatment of various diseases and are being developed as therapeutic agents during the recent past few years

Here by all the students and faculty members are invited to read and contribute to ''QUEST'' to propagate the idea of knowledge gaining by sharing.

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Research News: About 400 words (1 page)
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Line Spacing: 1
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References: 1) In text citing, S No, Superscript.
2) Author's name (s), *Journal name*, **Volume No**, Page No**,** (year).
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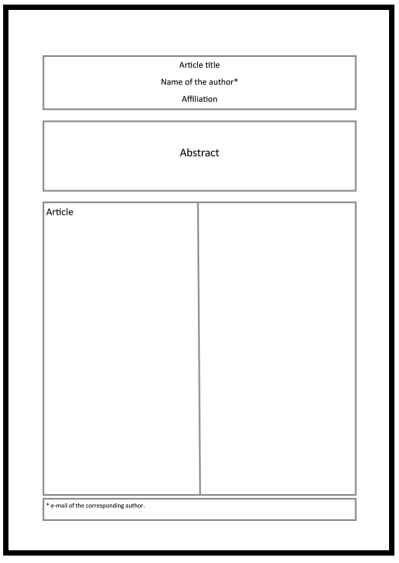

Fluorescent biosensors light up high-throughput metabolic engineering

Genetically encoded fluorescent biosensors allow researchers to see how products form in real time in microorganisms, and to test billions of candidates at a time

Synthetic biologists are learning to turn microbes and unicellular organisms into highly productive factories by re-engineering their metabolism to produce valued commodities such as fine chemicals, therapeutics and biofuels. To speed up identification of the most efficient producers, researchers describe new approaches to this process and demonstrate how genetically encoded fluorescent biosensors can enable the generation and testing of billions of individual variants of a metabolic pathway in record time.

Biotechnologists that tinker with the metabolism of microorganisms to produce valued products look at the engineering process through the lens of the so-called 'design-build-test cycle.' The idea is that multiple iterations of this cycle ultimately allow the identification of combinations of genetic and metabolic elements that produce the highest levels of a desired drug or chemical. Key to the cycle's efficiency, however, is the ability to construct and test the largest number of variants possible; in the end, only a few of these variants will produce the product in industrially attractive amounts.

Bioengineers thoroughly understand how metabolic pathways work on the biochemical level and have a plethora of DNA sequences encoding variants of all of the necessary enzymes at their disposal. Deploying these sequences with the help of computational tools and regulating their expression with an ever-growing number of genetic elements, gives them access to an almost infinite pool of design possibilities. Similarly, revolutionary advances in technologies enabling DNA synthesis and manipulation have made the construction of billions of microorganisms, each containing a distinct design variant, a routine process.

Source: www.sciencedaily.com

-Contributed by Krishna Saraiya IGBT IV , Dipika Patel

From prediction to reality: a history of the search for gravitational waves

- **1915 -** Albert Einstein publishes general theory of relativity, explains gravity as the warping of spacetime by mass or energy
- **1916 -** Einstein predicts massive objects whirling in certain ways will cause spacetime ripples—gravitational waves
- **1936 -** Einstein has second thoughts and argues in a manuscript that the waves don't exist—until reviewer points out a mistake
- **1962 -** Russian physicists M. E. Gertsenshtein and V. I. Pustovoit publish paper sketch optical method for detecting gravitational
- waves—to no notice
- **1969 -** Physicist Joseph Weber claims gravitational wave detection using massive aluminum cylinders—replication efforts fail
- **1972 -** Rainer Weiss of the Massachusetts

Institute of Technology (MIT) in Cambridge independently proposes optical method for detecting waves

- **1974 -** Astronomers discover pulsar orbiting a neutron star that appears to be slowing down due to gravitational radiation—work that later earns them a Nobel Prize
- **1979 -** National Science Foundation (NSF) funds California Institute of Technology in Pasadena and MIT to develop design for LIGO
- **1990 -** NSF agrees to fund $250 million LIGO experiment
- **1992 -** Sites in Washington and Louisiana selected for LIGO facilities; construction starts 2 years later
- **1995 -** Construction starts on GEO600 gravitational wave detector in Germany, which partners with LIGO and starts taking data in 2002
- **1996 -** Construction starts on VIRGO gravitational wave detector in Italy, which starts taking data in 2007
- **2002–2010 -** Runs of initial LIGO—no detection of gravitational waves
- **2007 -** LIGO and VIRGO teams agree to share data, forming a single global network of gravitational wave detectors
- **2010–2015 -** $205 million upgrade of LIGO detectors
- **2015 -** Advanced LIGO begins initial detection runs in September
- **2016 -** On 11 February, NSF and LIGO team announce successful detection of gravitational waves.

Physicists working with the Laser Interferometer Gravitational-Wave Observatory (LIGO) announced that after decades of effort they had detected gravitational waves—ripples in spacetime itself—set off by the explosive collision of two massive black holes. But which of the 1000 scientists who work on LIGO, a pair of gargantuan instruments, was the first to see the long-awaited signal?

His tale shows how elaborate plans devised to keep LIGO team members guessing whether a signal is real or a purposefully planted fake broke down, leaving one lucky physicist and, soon, the entire LIGO collaboration sitting on a thrilling secret.

Marco Drago wasn't in Louisiana or Washington, or even the United States. Instead, the 33-year-old postdoc from Padua, Italy, was at his office at the Max Planck Institute for Gravitational Physics in Hanover, Germany, where members of the LIGO team work on data analysis. There, Drago oversees one of four data "pipelines," automated computer systems that comb through the raw data coming out of the two detectors looking for potentially interesting signals. On 14 September 2015, while Drago was on the phone with a LIGO colleague in Italy, his pipeline sent him an email alert—of which he receives about one each day—telling him that both LIGO detectors had registered an "event" (a non-routine reading) 3 minutes earlier, at 11:50:45 a.m. local time. It was a big one. "The signal-to-noise ratio was quite high—24 as opposed to [the more typical] 10,".In fact, the signal was so strong that Drago didn't believe it was real—and with good reason. A gravitational wave from a distance source stretches space by an infinitesimal amount, and to detect that rhythmic stretching LIGO employs two gigantic optical devices called interferometers, which essentially act as gigantic rulers. To test the incredibly complicated devices, LIGO physicists have developed mechanical systems to give them a shake and "inject" a fake signal.

The signal Drago saw was so perfect it seemed too good to be true, he says. “No one was expecting something so huge, so I was assuming that it was an injection.”

Injections can be done in two ways: out in the open when researchers are tuning up the machines and secretly when they are taking data. Those latter “blind injections” are meant to keep researchers on their toes. Only four LIGO leaders know when such injections are made, and that information is supposed to be revealed only after a potential signal has been thoroughly scrutinized and written up for publication. That’s how things unfolded in 2010, when LIGO researchers learned at the last minute that a possible signal was in fact a blind injection. So if all had gone as anticipated, Drago might have simply noted the alert and carried on as usual, assuming the truth would come out in the end. Drago knew that the injection system was not supposed to be working. He immediately set out to verify that and ended up alerting the entire collaboration to the signal.

-Contributed by Krishna Saraiya
IGBT IV, Dipika Patel

Using light to control protein transport from cell nucleus

Light can be used to control the transport of proteins from the cell nucleus with the aid of a light-sensitive, genetically modified plant protein. Biologists working in the field of optogenetics have now developed such a tool. The researchers employed methods from synthetic biology and combined a light sensor from the oat plant with a transport signal. This makes it possible to use external light to precisely control the location and hence the activity of proteins in mammalian cells.

Eukaryotic cells are characterised by the spatial separation between the cell nucleus and the rest of the cell. "This subdivision protects the mechanisms involved in copying and reading genetic information from disruptions caused by other cellular processes such as protein synthesis or energy production," explains Prof. Eils, Director of Heidelberg University's BioQuant Centre and head of the Bioinformatics Department at Ruperto Carola and the DKFZ. Proteins and other macromolecules pass through the nuclear pore complex into and out of the cell nucleus in order to control a number of biological processes.

While smaller proteins passively diffuse through the nuclear pores, larger particles must latch onto so-called carrier proteins to make the trip. Usually short peptides on the protein surface signal the carriers that the protein is ready for transport. This signal is known as the nuclear localization signal (NLS) for transport into the nucleus, and the nuclear export sequence (NES) for transport out of the nucleus. Artificially inducing the import or export of selected proteins would allow us to control their activities in the living cell. The Di Ventura lab has specialised in optogenetics, a relatively new field of research in synthetic biology. Optogenetics combines the methods of optics and genetics with the goal of using light to turn certain functions in living cells on and off. To this end, light-sensitive proteins are genetically modified and then introduced into specific target cells, making it possible to control their behaviour using light. The hybrid LOV2-NES protein can be attached to any cellular protein and used to control its export from the nucleus using light.

The property of light-induced structure change can now be used specifically to synthetically control cellular signal sequences -- like the nuclear export signal (NES). Dominik Niopek first developed a hybrid LOV2-NES protein made up of the LOV2 domain of the oat and a synthetic nuclear export signal. In the dark state, the signal is hidden in the LOV2 domain and not visible to the cell. Light causes the structure of the LOV2 to change, which renders the NES visible and triggers the export of the LOV2 domain from the nucleus.

The researcher and his team demonstrated this using the p53 protein, a member of the family of cancer-suppressing proteins that monitor cell growth and prevent genetic defects during cell division. According to Roland Eils, p53 is switched off in a number of aggressive tumours by harmful genetic mutations that allow the tumour cells to reproduce uncontrollably. Using the LOV2-NES protein, the Heidelberg researchers were able to control the export of p53 from the nucleus using light to control its gene regulatory functions. “This new ability to directly control p53 in living mammalian cells has far-reaching potential to explain its complex function in depth.

The hope to uncover new clues about the role of possible defects in p53 regulation related to the development of cancer. The researchers are convinced that their new optogenetic tool can also be used to make important discoveries on the dynamics of protein transport and its influence on cell behaviour . The development of innovative molecular tools is therefore the key to understanding basic cellular functions as well as the mechanisms that cause illness.

Source: www.sciencedaily.com

-Contributed by Krishna Saraiya IGBT-IV, Dipika Patel

Former insights into pathophysiology and treatment of Nephrotic syndrome: A short review

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Abstract

Nephrotic syndrome (NS) is a chronic kidney disorder, distinguished by modifications of glomerular filtration barrier, resulting in its incapability to control the urinary protein loss. NS is a pathological entity identified by massive proteinuria which can lead into mortal infections, thrombosis, and edema due to significant protein loss. Information about principal cause of a syndrome is necessary for accepting its mechanism and for its sufficient classification, prediction, and management. Currently, the etiologies of NS have been revealed due to various acquired as well as genetic defects and its progressive forms can lead to chronic and end-stage renal disease. Foremost breadth of view about pathophysiology and treatment of Nephrotic syndrome are reviewed.

Introduction

During of the 20th century attempts were made in the medical literature to distinguish nephrosis (i.e. kidney disease distinguished by exudation and proliferation) from nephritis (i.e. nephritis). But, when it was noticed that nephrosis is neither a single disease, nor a group of related diseases, the word "nephrosis" was replaced by "nephrotic syndrome"[1]. Clinically nephrotic syndrome (NS) features develops into rigorous proteinuria, hypoalbominemia, edema and hypercholesterol conditions. These circumstances are closely related to foremost structural and morphological changes in glomerular epithelial cells, also named as "podocytes". Podocytes are extremely specific cells with abundant foot processes that cover up the external aspect of the glomerular basement membrane (GBM). One of the vital purposes of kidney for the period of prime urine formation is ultrafilteration of plasma protein. Ordinary filtration task of the glomerulus relay on the structural and functional reliability of the filtration barricade, that is the chief target of numerous innate and acquired glomerular dysfunctions, distinguished by nephrotic syndrome (greater than 3.5 g protein per day) and swift development to end stage renal disease (ESRD)[2]. In the primary NS of size around 60-280 KDa plasma proteins are lost that makes remarkable changes in plasma protein level. Etiology says, NS is caused due to two main reasons (1) acquired (due to toxins or infection), and (2) genetics[3]. The total ontonic pressure and plasma protein level decides the secondary effects of NS, where plasma protein level goes up to 750g/l causing extension in plasma volume. In NS, there is thickening of the foot process, but the remaining of the cell generally is conserved[4]. Endothelial cells possess many outlets that are 65 to 95 nm in diameter, called fenestrae, which form a substantial barrier for passageway of macromolecules from plasma into the renal tubule. Electron microscopy information leads to the recognition of negatively charged particles in the GMB, which prevent the passage of anionic macromolecules like

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albumin[5].

Epidemiology

NS can influence any age group, both children and adults as primary or secondary form of which 62% to 80% are glomerulonephritis cases, where as others are of secondary nephropathy. In US, occurrence of NS is 3-4 cases per 100,000 children per year[8]. Increasingly this has been gone up to 16 cases per 100,000 children. When compared it has been found more frequent among boys than girls of juvenile age groups, but once they reach at puberty there is no such noteworthy difference among genders. NS has been more frequently observed at the age of 2-14 among children. Research proved Enlarged prevalence and extreme disease condition in African American and Hispanic populations[6]. There are also differences in epidemiology between the colours, the disease is more general in black than in white by a ratio of 2 to 1.The incidence data also states knowledge related to the majority widespread way that symptom develops in patients with NS as unprompted remission happens in up to 25% to 35% of cases during the initial year of the illness[7]. On the other hand, this improvement is not classic as some 55% to 65% of patients dies and / or expand to unrelieved renal failure 7 to 14 years after this remission. The main causes of death are cardiovascular, as a result of the chronicity of the syndrome, and thromboembolic accidents[8].

Pathophysiology

In NS, the pathophysiology of normal glomerular filtration function is strongly interrupted, resulting in severe-range proteinuria and hypoalbumina conditions. Reports showed role of immune pathogenesis where defect in T-Cell occurs through various circulating factors such as cytokines and other molecules[9,10]. On the whole, the glomerular filtration barrier is made of three consecutive layers, scheduled from capillary side to bowman's space side: Fenestrated endothelium negatively charged basement membrane to prevent the passage of large anionic molecules, visceral epithelial called as podocytes, which contains small pores with a fixed size with radius of around 30 to 50 amperes connecting adjacent foot processes are bridge by slit diaphragms and further maintain structural and function integrity of GMB[11]. In NS, the glomeruli are unable to filter back. NS pathophysiology revel protenuria, here the glomeruli are affected by inflammation or hyalinization and are unable to filter back albumin or other immunoglobulins back into blood rather these molecules pass through the membrane and are found in urine. Albumin is the major blood protein that regulates plasma ontonic pressure which causes increase in hepatic lipoprotein and transcapillary water level which later on causes the hyperlipidemia and edima conditions linked with NS. The actual mechanism by which this glomerular membrane gets damaged in primary and secondary disease is unknown, but reports chains the role of T-cells in up regulating circulating factors or down regulating inhibitory factors in reaction to unrevealed immunogens and cytokines[12].

Other probable facts involved in pathophysiology of NS can be either hereditary defect in proteins that are essential to the slit diaphragms such as Nephrin and podocin or activation of cell complementary system causing damage and loss of the negatively charged groups attached to proteins of the GBM.

A diverse metabolic consequence of proteinuria includes, Infection, Hypocalcemia and bone abnormalities, Hypercoagulability and Hypovolemia. During infections patients are more susceptible to Varicella infection along with *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Escherichia coli*. The most common infectious complications are bacterial sepsis, cellulitis, pneumonia, and peritonitis[13]. NS patients are very frequently affected by hyopocalcemia conditions caused by low serum albumin level; on the other hand low bone density and abnormal bone histology are also reported.

Urinary losses of vitamin D–binding proteins with subsequent hypovitaminosis D are one of the reason of such circumstances where reduced in intestinal calcium absorption occurs[14]. It is probable that long duration of either this syndrome or its treatments are the significant risk factors for bone disease in these patients. Venous thrombosis and pulmonary embolism are eminent complications of NS, in these patients urinary loss of anticoagulant proteins, like antithrombin III and plasminogen, beside synchronized raise in clotting factors, particularly factors I, VII, VIII, and X causes conditions such as Hypercoagulability[22].

A report by Mahmoodi et al confirmed the increase in venous thromboembolism (VTE) and arterial thrombotic events together with coronary and cerebrovascular ones with 10 to 15 times higher effect in NS patients compare to normal ones. Acute renal malfunction may point to a fundamental glomerulonephritis however it is more frequent causes of hypovolemia or sepsis. All these consequences finally results to Hypertension connected fluid retention and reduced kidney function which may develop in patients with chronic end stage renal disease[22,23].

Signs and Symptoms

The universal sign and manifestation of NS are swelling, weight gain, fatigue, blood clots, and infections where as some patients may develop kidney failure. Due to increase in protein excretion the urine in the toilet bowel may direct to frothy appearance[25]. This injure where protein usually leak in the urine in more quantity, reduces the total blood protein level. In view of the fact that the protein in the blood prompts the flow of liquid in the bloodstream, due to low protein level this fluid leak out of into tissues, causing swelling, and called edema[15]. The swelling is mainly visible in legs and around eyes when the patients first get up in the morning, in due course of time this swelling may be there all the time and arise in other body parts too along with rapid weight gain[16]. Very less number of patient's are found to have weight loss and this may be due to malnutrition or an principal circumstances, such as badly controlled diabetes mellitus, a chronic viral infection, or cancer. Gradually NS develops in kidney dysfunction, with no or less symptoms at early stage but conversely kidney function continues to worsen finally developing end stage renal disease symptoms, with shortness of breath, weakness and easy fatigability (from anemia) and loss of appetite[17]. The concentration of lipids especially cholesterol and/or triglycerides can become greatly elevated in patients causing increase in risk of coronary artery disease[18]. Patients with NS are at greater risk of blood clots in the veins or arteries which travel through

lungs which leads to dangerous and fatal stage. Patients with severe NS are at increased danger for infections, even though the reasons for this are not well understood. Simple test includes urine visualization where urine foams more than normal because of the quantity of protein in it. Diagnosis may also require a kidney biopsy[29].

Treatment and management

Patients who show positive with signs and symptoms of intense assault are supposed to be treated straight away in an intensive care setting. Current studies confirmed the effectiveness of intravenous theophylline in dropping the period and intense leaky phase of an acute NS. Different vasopressors drugs, for example, 260 mL of a 20% albumin-containing solution, given over 20-60 minutes at intervals determined by clinical status, which have been found to be more successful in maintaining hemodynamic stability among patients[30]. Corticosteroid therapy to counter the inflammatory triggers has now a day's occasionally stopped or minimized as it has been believed that steroids may be damaging to patients who face more frequent attacks and even the affect steroid course in subsequent episodes is uncertain. Many people who go through more severe attacks require mechanical ventilation because of flash pulmonary edema[19,20].

The main goals of cure are to reduce symptoms, avoid complications, and hinder end-stage renal damage. Here are few commonly used treatments enlisted below used to control NS by treating the disorder that is causing it.

- Use of ACE inhibitors i.e. Angiotensin-converting enzyme, to diminish proteinuria, and decrease the threat of evolution to renal disease in persons with NS. In some patient's steroids are given along with ACE inhibitors and maintaining blood pressure at or below 120/80 mmHg to improve response. The suggested dose is unclear; the actual dosage varies from patient to patient. Keep blood pressure at or below 130/80 mmHg to delay kidney damage[21].
- Treatment with corticosteroids remains different among adults and children and is more clearly proved that children respond well compare to grownups, in some patient's it is beneficial while others do not respond at all. Previous studies prove that patients with minor rigorous glomerular changes responded well to steroids treatment. It is recommended that family physicians must consult with nephrologists whether treatment with corticosteroids is sensible, on the contrary the indecisive benefits and chance of adverse effects. Use of alkylating agents has few less proof for improving disease condition, but may be considered for patients who do not respond to corticosteroids[22].
- Studies are going on to inspect the benefits and problems of lipid-lowering treatments in NS. A number of confirmations suggested an enlarged hazard of atherogenesis or myocardial infarction in patients with NS, perhaps connected to increased lipid levels. Lipid lowering treatment is used to treat high cholesterol to decrease the risk of heart and blood vessel problems and for that medication to decrease cholesterol and triglycerides are usually needed[23].
- Along with all these therapies doctors recommended few antibiotic and anticoagulating treatments deepening upon patients response to NS. A low-salt and low-protein

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Current Status on Metal Based Drugs

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Abstract : Now a day's metal based drugs or metallo drugs, have shown promising results in the treatment of various diseases such as diabetes, ulcer, rheumatoid arthritis, inflammatory and cardiovascular diseases etc. in addition to cancer. It was observed that in certain cases the interaction between enzymes and heterocyclic compounds (ligands) was affected by the presence of certain trace amount of metal ion, since metal ions are required in trace amount to form complexes between the ligand molecule and enzymes. Formation of metal complexes results into wide variety of coordination spheres, oxidation states and redox potential, will alter the kinetic and thermodynamic properties of the complexes towards biological receptors. Thus, metal complexes are responsible for drastic change in the biological properties of ligands. Metal complexes exert their biological effect by inhibition of enzymes, interaction with intracellular biomolecules, enhanced lipophilicity and alteration of cell membrane functions etc. Therefore, the present review describes the importance of some metal ions and metal based drugs having promising results in the treatment of various diseases and are being developed as therapeutic agents during the recent past few years.

Introduction

Metals and metal complexes have played key role in the structure and functions of all life forms present on Earth. It can be in the form of metal ions (such as K^{+}, Fe^{+2} and Fe^{+3}), composite ions (e.g. molybdate), coordination compounds (like *cis*-platin and carbonyltechnetium), or inorganic molecules such as CO, NO, O_3.

Metal ions play important role in biological processes in the human body for example, Zn (II) and Cu (II) ions are the second and third most abundant transition metals in humans. They are found either at the active sites or as structural components in most of enzymes. Cobalt is present in vitamin B_{12}, a co-enzyme that plays significant roles in many biochemical processes[1, 2]. Some of the transition metal ions are effective

therapeutic agents especially when coordinated to a ligand to form metal complexes. In addition to that metal such as platinum, silver, gold, bismuth, antimony, vanadium, iron[2, 3] are used in chemotherapy for treatment of diseases such as anticancer, antimicrobial, antiarthritic, antiulcer, antiprotozoal, antidiabetic and antimalaria respectively. Besides this, other metal ions like Fe, Mg and Co have diverse role in various biological system such as; magnesium porphyrin complex of chlorophyll is used in green plants for photosynthesis, - cobalt in the coenzyme B_{12} for the transfer of alkyl groups

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from one molecule to another molecule.
The amount of metal ions present in the human body is around 0.03% of the body weight. Low or high metal ion concentrations may be harmful for the human.

Heterocyclic molecules (ligands) having electron donor atoms like N, O, S, and P etc. may form coordination bond with various metal ions. Formation of chelation causes drastic changes in the biological properties of ligands and metal ion. In many cases it causes additive effect of both metal ion and ligand[4-6]. Various mechanisms have been reported for their biological action including inhibition of enzymes, interaction with intracellular biomolecules, enhanced lipophilicity, alteration of cell membrane functions and arrest of cell cycle etc.

Thus, the study of metal-based drugs is broadening rapidly, and a variety of different and distinctive metal based drugs are reported so far, as mentioned below :

(i) Metal compounds as anti-cancer agents:
Platinum drugs : *cis*platin contains a square-planar geometry in which platinum (II) is a central metal, coordinated to two ammonia ligands and two chloride ligands with a *cis*-conformation.

- iron porphyrin complex of hemoglobin is used in red blood cells (RBCs) for oxygen transportation and storage of oxygen,

Mode of action : *cis*platin acts through its interaction with DNA. The compound (*cis*-platin) is administered by injection into the bloodstream and is believed to remain in its neutral state until after it crosses the cell membrane where the chloride ligands are displaced by aqua ligands affording cationic compounds. These cationic aqua derivatives react with the bases on DNA, most commonly with the N7 of purine bases, which displace the aqua/chlorido ligands. A bifunctional adduct is formed between the cisplatin unit and two adjacent bases on the same strand. Other platinum drugs approved for worldwide clinical uses are : carboplatin, oxaliplatin, nedaplatin, heptaplatin and lobaplatin. Some of are under commercial development like satraplatin, picoplatin miriplatin and aroplatin. Some of the Trans and polynuclear platinum drugs have also shown some anticancer activity[7]: These classes of drugs show potencies similar to that of cisplatin and, perhaps more importantly, are active against cisplatin-resistant cell lines.

In addition to platinium, other metal ions used are Ruthenium, Titanium and gallium for the formation of metal based drugs.

(ii) Metal compounds as anti-diabetic agents:
Vanadium complexes such as bis(α-furancarboxylato) oxovanadium(IV), bis (pyridine-2-carboxylato), oxovanadium (IV) [$VO(pic)_2$], bis(α-furancarboxylato) oxovanadium(IV), Vanadyl complexes with maltol (3-

hydroxy-2-methyl-4-pyrone) and kojic acid (3-hydroxy-2-hydroxymethyl-4-pyrone) etc. possess insulin mimetic activity and low toxicity profile, have been proposed for clinical use in humans[6, 8, 9].

(iii) Metal compounds as antibiotics :

Most of antibiotics do not need metal ions for their biological activities, however, some of the antibiotics such as bleomycin, streptonigrin and bacitracin that require metal ions to function properly. The coordinated metal ion in these antibiotics play an important role in maintaining proper structure and functions of such antibiotics. Removal of the metal ions from these antibiotics can cause changes in structure and function of these antibiotics. Metalloantibiotics can interact with different kinds of biomolecules including DNA, RNA, proteins, receptors and lipids rendering them unique and specific bioactivities[10].

(iv) Metal compounds as anti-HIV agents :

Vanadium complexes are well documented to have therapeutic applications. Recent studies showed that oxovanadium (V_2O_3) complexes of thiourea and vanadium substituted olyoxotungstates exhibit potent anti-HIV properties towards infected immortalized T-cells[11, 12].

(v) Metal compounds as anti-inflammatory agents :

A large number of transition metal complexes of tolmetin, naproxen, ibuprofen, flufenamic acid, indomethacin, diclofenac, aspirin, piroxicam etc. have been reported as anti-inflammatory gents. Vanadium complexes with the NSAIDs - tolmetin, ibuprofen, naproxen and aspirin have been recently prepared and evaluated for anti-inflammatory activity. Some vanadyl complexes of anti-inflammatory drugs containing carboxylate ligands have shown promising results[13]. The complexes such as Gold(I) thiomalate [myocrisin (Autm)n], gold(I) thioglucose [solganol (Autg)n] and auranofin [2,3,4,6-tetra-*o*-acetyl-1-thio-β-D-glucopyranosato-(S)-triethylphosphine gold(I)] have been successfully used over many years for the treatment of rheumatoid arthritis[14-16].

(vi) Metal compounds as antimanic agent :

Lithium salts have proved clinical effectiveness for alcohol abuse and aggression, epilepsy, tardivedys-kinesia, schizophrenia, Huntington's chorea, premenstrual syndrome, migraine and cluster headaches. Lithium carbonate may be used as in psychiatric disorders such as pathological aggression and reduction in acute or attempted suicide is also recognized[17, 18].

(vii) Metal compounds as antimicrobial agents :

Silver and silver containing compounds such as $[Ag(hino)]_2$ (where hino = 4-isopropyltopolone) and silver(I) complexes of (R)-(+)- and (S)-(-)-2-pyrollidone-2-carboxylic acid, Silver sulfadiazine etc. are used as antimicrobial agents[19, 20].

(viii) Metal compounds as antiparasitic agents :

Metal complexes of gold, platinum, iridium, palladium, rhodium and Osmium have been reported to have activity against a variety of trypanosomatids. Chloroquine complex of transition metal ruthenium, $[RuCl_2(CQ)]_2$ has been found to be 2 to 5 times more active than chloroquine diphosphate in *in-vitro* without any acute toxicity[21].

(ix) Metal compounds as antiulcer agents :

Bismuth compounds such as colloidal bismuth subcitrate, bismuth subsalicylate and ranitidine bismuth citrate are the most widely used drugs for the treatment of variety of gastrointestinal disorders such as diarrhea, dyspepsia and peptic ulcers because of their antacid and astringent properties[22].

(x) Metal compounds as antihypertensive agents :

NO compound have varied biological role in human physiology has facilitated the development of NO containing metallopharmaceuticals. They have role in human physiological processes like neurotransmission, blood pressure regulation and immunological responses. Sodium salt of nitric oxide [$Na_2[Fe(CN)_5NO].2H_2O$] is used for the treatment of hypertensive patients. Ruthenium complex of nitric oxide [*trans*-$[Ru(NH_3)_4P(OEt)_3(NO)](PF_6)_3$] has shown similar antihypertensive activity but reduced toxicity with compared to sodium nitroprusside[23]. The peroxynitrite plays a role in many other pathological conditions such as sepsis, arthritis, diabetes and epilepsy. Ruthenium polyamino carboxylate complexes are efficient NO scavenger [24-26] and demonstrating their therapeutic potential.

Conclusion

Thus, the role played by metal complexes as therapeutic agents is becoming important in the field of medicinal chemistry. A large number of metal complexes are formed by the use of different metal ions and organic ligand of interest. Metal complexes like *cis*platin has proven to be highly effective chemotherapeutic agents for treating various types of cancers.

The use of transition metal complexes offers a great diversity in their action; they do not only have anti-cancer properties but have also been used as anti-inflammatory, anti-infective and anti diabetic compounds. Besides their certain limitations and side effects, metal complexes are the most widely used chemotherapeutic agents and make a large contribution to medicinal therapeutics.

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