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Recent Research at the Intersection of Science & Technology

Editors:

Dr. Ved Patki

Dr. Kailash Nemade

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PREFACE

Discipline boundaries have been systematically developed and established over the last century which reflects some of the apparent differences between the science and technology. Interdisciplinary research has been a growing paradigm in science and technology for the past few decades because of the increase in the complexity of scientific and technological innovation. Analyses of complex information systems may require the crossing of departmental boundaries in order to generate new knowledge.

Today the whole world is contributing significant time and efforts to advanced research because it holds the keys to the future advancements and enhancement of resources for society. New advancement in interdisciplinary research has to be infused with innovative techniques, play a decisive role in advancing wellbeing of the society. These efforts will provide a common platform to the scientists, researchers and academicians to communicate and share their productive outcomes. Interdisciplinary research activities are said to be research when experts or researchers from diverse ground work together within the limits of their own discipline and they are adopting an interdisciplinary approach.

The purpose of interdisciplinary research activities is to reduce the gap between subject areas and maximize the mutual sharing of knowledge and ideas. Sometime the complicated research problem cannot be investigated by an individual discipline and it necessitates the collaboration of people of diverse expertise across a range of discipline together to achieve the research goal. The main objective of this book is to exchange the recent ideas and innovations in various fields along with research methodology which will be helpful for betterment in each and every field of studies.

This book is primary attempt to encompass of recent developments in science and technology. Also, book comprises discussion on various interdisciplinary from life sciences to chemical sciences and physical sciences.

- Editors

Dr. Ved Patki

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CONTENT

CHAPTER 1

SPIDERS AS A POTENTIAL BIOINDICATOR OF SATPURA FOREST RANGES HEALTH

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Spiders have been increasingly used as environmental and ecological indicators in conservation and ecosystem management. Bioindicators are used for conservation by means of spatial comparisons of a site value, or monitoring of ecosystem recovery or response to management. Spiders are characterised by their selection of quality habitats and guild response to environmental change.

Spider is a group of invertebrates belonging to the class Arachnida of phylum Arthropoda, sub-phylum Chelicerata (eight legs). Phylum arthropoda consists of insects, arachnids and crustaceans, the animals that possess jointed appendages and chitinous exoskeleton. Like all arthropods, arachnids have an exoskeleton and internal cartilage-like tissue. Major developments in spider evolution include the development of spinnerets and silk secretion, as well as different adaptations for its use. Among the oldest known land arthropods are Trigonotarbids, members an extinct order of spider-like arachnids. At one stage the oldest fossil spider was believed to be *Attercopus* which lived 380 million years ago during the Devonian. (Penney and Seldon, 2011). Spiders are generally invertebrates predators, the great majority feed principally on insects (Marc *et al.,* 1999). Although Spiders have uniquely predatory habits, they do not constitute a homogeneous functional group and exhibit significant behavioral diversity in relation to different predation strategies, dispersal mode and ability to resist adverse ecological conditions (Marc *et al.* 1999).

Morphological Character (Tikader, 1982):

The body of the Spider divisible in to a distinctive cephalothorax and abdomen, joined together by a narrow pedicel. The cephalothorax is covered dorsally by a hard sclorotic shield the carapace, and ventrally by sternum. The anterior articulates movably with the labium. The legs are articulates in the plural membrane between the lateral edges of the carapace and sturnum. On the cephalic region are present six to eight eyes. The eyes are generally of two kinds, *viz*, black or diurnal and white or nocturnal eyes. When only one type is present, the condition is described as homogenous, in contrast to heterogeneous, when both the type are present. The eyes are usually arranged in double row, *viz*, the anterior row and posterior row. Each row usually contains four eyes. The eye row is described as recurved, when concavity is turned forward as in text-fig.1.1

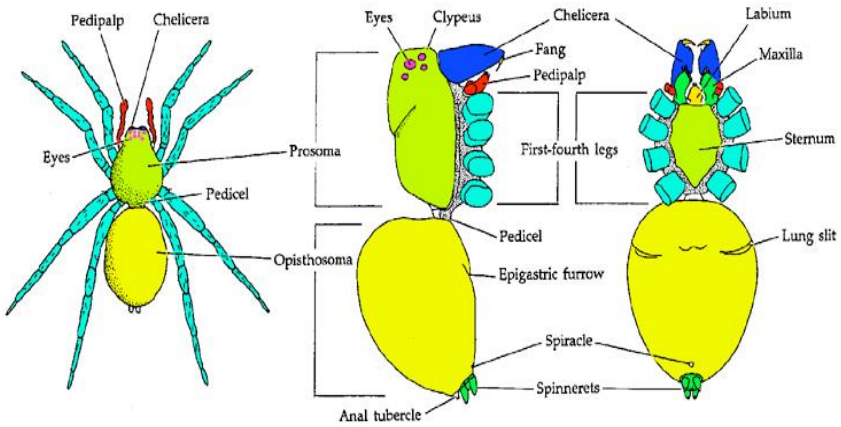

Figure 1: Morphology of Spider

Seasonal family composition:

Family compositions were determined for different habitat in Satpura Forest. On an annual basis, the family composition of winter active spiders on the trees was predominantly Aranids, Salticids and other families. the most abundant species is *Neoscona mukharji*.

Spiders are well documented as potential bioindicator in various ecosystems and their role in the dynamics of insect pest population controlled is well known, therefore Spiders can be used in designing future Biological Monitoring Program (BMP). Spiders act as generalist predators in the forest ecosystem. Species rich Spiders community is able to regulate prey density.

Vegetation structure is important for web building, sexual singling, ovoposition and over wintering.Spiders must anchor their pray capture device to the appropriate substratum and complex habitat provided appropriate site for greater range of sizes and types of web. Spiders find refuge from predators in spatially complex habitats (Gunnarson, 1990) However habitat selection in general is affected by biotic (e.g. Resource availability, quality, competition / interferences) and abiotic factors (e.g. Humidity, Temperature, Habitat structure). Alteration in vegetation structure is expected to facilitate changes in arthropods. Because Spiders depend heavily on arthropod prey, dynamic shifts in the prey base likely limit the spider assemblage from the bottom up. (Uniyal and Hore, 2008).

Spiders like many invertebrates, receive little attention from the conservation community. This may be due to fear and dislike of their appearance, behaviour or venomous nature; the fact that most Spiders are probably widely dispersed and not presumed to be threatened; or because relatively little is known about the distribution and abundance of these creatures.

Amravati district boasts of dense forest cover of 1428 Sq.km. It includes the famous widely spread satpuda forest ranges. The vegetation consist of Sal trees, *Lantena camera, Acacia leucopholia, Agle marmelos, Annona squamosa, Butea sperba* etc., but now a days due to human entrenchment and deforestation, the forest has been destroyed at large level. Disturbance to any factors of ecosystem may cause damage to whole ecosystem, so to study one of the factors from this ecosystem. As the Spiders are the natural insect controller, so spider population provide ecological states of the forest. Biotic properties of ecosystem are affected by Plant diversity. Spiders communities is influence positively by modifying important habitat and microclimate.

As per my experience in study area that the orb weaver *Nephila Banana* aggregates in areas of high prey density and the relationship between increased insect abundance and greater spider number have been shown in a number of previous visit of study area. Furthermore, field experiments conducted in enclosures have shown the web building spiders leave areas of low prey abundance and tend to remain where areas of prey captures are greater.

The aim of the present study is to assess the diversity and habitat association of Spiders and to examine the role of spiders as a potential bioindicator of the Satpura forest health with spiders assemblage. More specifically, I test whether vegetation, habitat, Pre density, Microclimate are good predictor of Spiders diversity as well as forest heath. In this Survey I present one family of Spiders an ecological indicator (Bioindicator) of habitat condition i.e. family Arachnidea in the Satpura Forest.

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CHAPTER

2

HERBAL ALTERNATIVE FOR SYNTHETIC CASTRATION

Dinesh Dabhadkar

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Introduction:

Castration in males is a procedure by which the person loses the function of his testes, thereby resulting in loss of libido and infertility. In ancient India, castration was performed on strong men to convert them into eunuchs, who were then posted to guard the women's quarters. In some countries sex offenders are sentenced to castration.

Castration is performed by two different procedures: In surgical castration, the testicle is surgically removed which causes permanent effects. In medical or chemical castration, drugs are given at regular intervals to reduce testosterone levels in the body, thereby reducing sexual arousal and resulting in infertility. Thus, although the term 'chemical castration' sounds very scary, the actual process involves the administration of only a few drugs to the person. Although chemical castration for sex offenders, including pedophiles, has been adopted in some states of the USA and some European countries, it is still a controversial issue in India. The first case of chemical castration in Asia was recently cleared by a South Korean court, while other countries, including Malaysia, are pushing for a similar sentence.

Growing human populations around the world, especially in developing and underdeveloped countries, have detrimental effects on life support systems on Earth. Traditionally, plants have been used to treat a variety of ailments. The increasing importance of phytochemicals in men has been noted. The castration capacity of the plant has been noted in some animal specimens. The anti-reproductive effects of the plant and its active compounds have potential clinical relevance in the development of reversible male herbal castration medicine (Ogbuewu *et al*., 2011).

Herbal castration is a procedure wherein medications are administered to reduce testosterone levels in male. The recent surge in rape cases has reiterated a fresh demand for introduction of herbal castration for rapists in India. In addition, some wives are urging their husbands to reduce their libido.

There are already many medical treatments that act as anti-androgens and their use is approved; however, in recent years, the demand for complementary and alternative

therapies has increased, and this has led to an increase in interest in the development and use of anti-androgen therapies derived from more plants. This is particularly relevant because some of the drugs currently in use have been found to have sub-optimal efficacy in clinical practice, and many patients are eager to try 'natural' or 'alternative' approaches to artificially obtained compounds. This review provides an overview of the terms, indications, and uses of anti-androgen drugs with a particular focus on innovative interests in the ancient field of plant-derived therapies.

There are no much more herbal castration techniques available. However, there are certain herbs like black cohosh, dong quai, chaste berry and saw palmetto that can lower testosterone levels to an extent. Therefore, the present chapter is small effort to gain insight in the knowledge of traditional medicine of castration.

Interdisciplinary relevance:

This work will have immense interdisciplinary relevance if the active components responsible for castration activity are isolated from the plant extract .These can be formulated as herbal castration drug of plant origin by the Pharmaceutical sector.

International status:

Castrations after the onset of puberty will typically reduce the sex drive considerably or eliminate it altogether. Castrated people are automatically sterile, as the testicles (for men) and ovaries (for women) produce the sex cells needed for sexual reproduction. Once removed the subject is infertile. The sound does not change. Some castrates report mood changes, such as depression or a more calm outlook on life, although these may be due to emotional changes, not due to chemical changes but to the effects of the process. Body strength and muscle mass may decrease somewhat. Body hair can sometimes fall out. Castration prevents male pattern baldness if it is done before hair loss. However, castration will not restore hair growth after the hair has already fallen out due to male pattern baldness (Hamilton, 1960).

Castration of non-human animals is intended for favoring a desired development of the animal or of his habits, or preventing overpopulation. The practice of castration has its roots before recorded human history (Cooke *et al*., 2011). Castration was frequently used in some cultures, mainly in South Asia, Africa, and East Asia for religious or social reasons. In some cases after battles, the victors cast their captive or defeated corpse to symbolize their victory and capture their "power". Castrated men - eunuchs - were often introduced into special social classes and used exclusively in staff jobs and palace homes: in particular,

the harem. In 1778, Thomas Jefferson wrote a bill in Virginia to reduce the penalty for rape, polygamy, or sodomy from death to castration.

National status:

An article in the Gulf Times in 2005 revealed the sex trade, mostly among Nepali boys, who were lured into India and sold into brothels in Mumbai, Hyderabad, New Delhi, Lucknow and Gorakhpur. One victim was lured from Nepal at the age of 14 and sold into slavery, locked up, beaten, starved to death and forcibly cast. He reported that he was kept in a brothel with 40 to 50 other boys, many of whom were cast. He fled and returned to Nepal. Two non-governmental organizations, one working with gays in Nepal, and one working to rescue and rehabilitate trafficked women and children, were cooperating to help and rescue these boys (Amlin, 2014). Temporary chemical castration has been studied and developed as a preventive measure and punishment for recurrent sexual offenses, such as rape or other sexual violence.

Not much of the research work have been done by researcher on herbal castration, so these is the argent need to emphasizes focus on such medically important aspect.

Significance of the herbal castration:

Natural products from medicinal plants, either as pure compounds or as certified extracts, provide unlimited opportunities for new drug leads due to the unmatched availability of chemical diversity. The discovery of a novel component from the medicinal plant under study may have pronounced pharmacological action on animal system and organ and may form the basis of development of therapeutic agent with better activity. Herbal castration reduces a person's ability to be sexually aroused and therefore reduces the likelihood of recurrence of sexual offenses in criminal cases.

Natural products from medicinal plants, either as pure compounds or as certified extracts, provide unlimited opportunities for new drug leads due to the unmatched availability of chemical diversity. The discovery of a novel component from the medicinal plant under study may have pronounced pharmacological action on animal system and organ and may form the basis of development of therapeutic agent with better activity. Since traditional medicinal plants knowledge is being lost at an alarming rate, this study will involve survey of the tribal belt of Melghat region helped to identify the tribal traditional wealth of medicinal plants.

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CHAPTER
3

STATUS, COMPLICATIONS AND RECENT ADVANCES IN MANAGEMENT OF SICKLE CELL DISEASE

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Introduction:

Sickle cell disease (SCD) is an autosomal recessive genetically transmitted haemoglobinopathy responsible for considerable morbidity and mortality. Sickle cell disorder is caused by a point mutation at 6th position in beta globin chain, valine substituting glutamic acid due to which in deoxygenated state the shape of erythrocytes change to sickle shape and also the fragility of cell membrane increases.

Figure 1: Point mutation in beta globin chain

Current scenario of SCD:

The sickle β globin gene is spread widely throughout Africa, the Middle East, Mediterranean countries, and India and has been carried, by population movement, to the Caribbean, North America, and Northern Europe. The frequency of sickle cell carriers is up to 1 in 4 in West Africans and 1 in 10 in Afro Caribbeans (Department of Health, 1993). Prior to 1952, no information was available about the existence of sickle cell disease in India. In 1952 it was recorded for the first time, simultaneously amongst the tribal population group of Nilgiri hills and laborers in the tea garden of Assam. Now it is firmly established that these genes harbor amongst different caste groups but with very high prevalence amongst scheduled castes, scheduled tribes and other backward communities (Baig *et al.,* 2004).

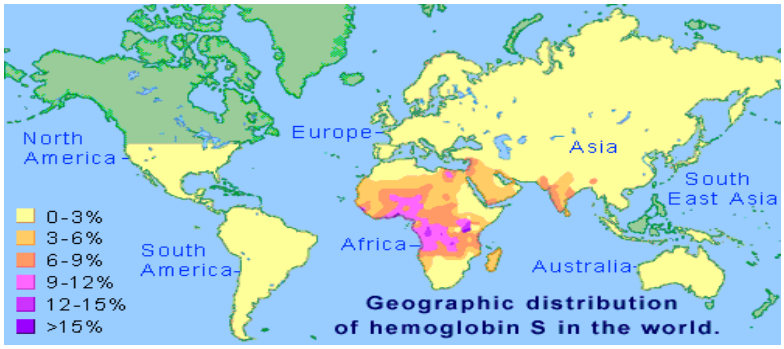

Figure 2: Prevalance of SCD over the World populations

The prevalence of sickle cell gene has been reported in many parts of India including Central India, where the prevalence in different communities ranges from 9.4% to 22.2% (Shukla & Solanki 1985). Available data indicates that SCD gene is widely spread in all districts of eastern Maharashtra (Vidarbha region), Northern Maharashtra (Satpuda range) and some parts of Marathwada region (Sharma 1983, Shukla & Solanki 1985.) Population genetic survey data has shown that the overall prevalence of sickle cell disorder in different tribal population in the state of Maharashtra is 10% for carrier state and 0.5% for the sufferers (Kate 2001).

Symptoms and complications associated with SCD:

Sickle trait serves as a protective mechanism against malaria (Kwiatkowski, 2005) Malaria is a deadly disease found in countries along the equator. People with sickle cell trait are protected from malaria while those with sickle cell anemia and normal hemoglobin are susceptible to it (Hedrick, 2011). The sickle gene has a genetic advantage that it protects heterozygous carriers from succumbing to endemic Plasmodium falciparum malaria infection (Nagel *et al.,* 2001).

Sickle-cell disease may lead to various acute and chronic complications, several of which have a high mortality rate (Malowany and Butany, 2012). All complications of Sickle Cell Disease can be traced to changes in the make-up of the RBC. Under certain conditions (i.e. acidosis, dehydration, infection, and low oxygen etc.) RBC's containing sickle hemoglobin become rigid, elongated, and sickle shaped (Fig. 3). Some RBCs sickle immediately, while others remain normal for hours before sickling. Most RBCs containing sickle hemoglobin can sickle and then unsickle. After repeated cycles of sickling and unsickling, the RBC's become irreversibly sickled. Sickled RBC's can become trapped within the blood vessels and thus interfere with normal blood flow (Fig. 4 and Fig. 5). This obstruction can lead to sudden pain anywhere in the body as well as cause damage to body

tissues and organs over time. Painful episodes are common complications in children with Sickle Cell Disease. Most episodes of sickle cell crises last between five and seven days (Lennette, 2000 and Ballas *et al.,* 2005). Although infection, dehydration, and acidosis (all of which favor sickling) can act as triggers, in most instance no predisposing cause is identified (Kumar *et al.,* 2009).

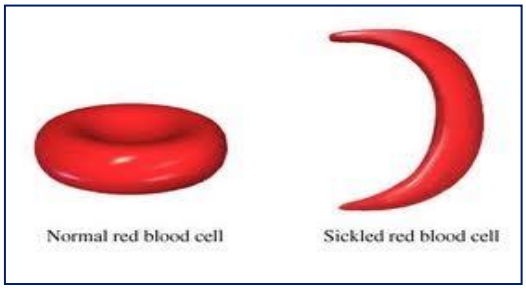

Figure 3: Normal and Sickled RBC

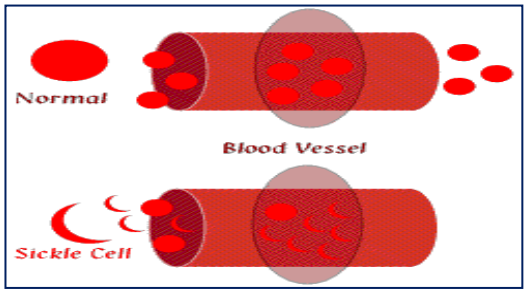

Fig. 4: Flow of Normal and Sickled RBC through blood vessels

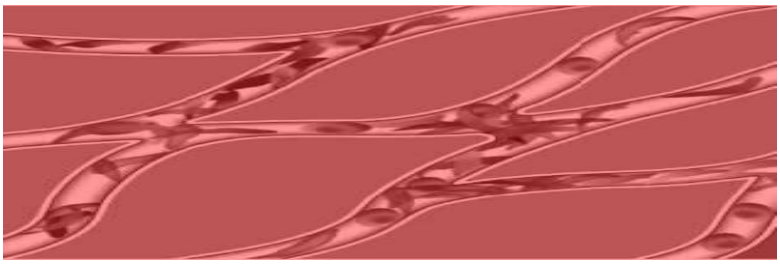

Figure 5: Vaso-occlusion crises- obstructed blood flow

When the sickled cells are unable to flow through small blood vessels they obstruct blood flow causing vascular occlusion (vaso-occlusion). Vaso-occlusion reduces blood flow to an area of the body resulting in pain. This can occur anywhere in the body, including fingers, arms, legs, ribs, abdomen, and organs such as the spleen, brain, and eyes. During infancy, vaso-occlusive crises (VOC's) are generally manifested as dactylitis or hand-foot syndrome (Fig 6.1). This is characterized by soft tissue swelling warmth and/or pain in the hands and/or feet due to ischemia (decreased oxygen) in these small bones. Dactylitis call be recurrent but usually does not occur after two or three years of age. The most common sites of pain in children over two years of age are the long bones, joints, back, and abdomen. Watson (1948) noted that symptoms appeared in infants only after concentrations of fetal hemoglobin (HbF) had fallen, established the notion of the beneficial effect of HbF on disease manifestations.

Normal red blood cells live 120 days in the blood stream, but sickle red blood cells last only 7-14 days. This means there are not enough healthy red blood cells to carry

oxygen throughout the body. When this happens, a person might have the following symptoms-fatigue, irritability, exercise intolerance, dizziness and lightheadedness, fast heart rate, difficulty breathing, pale skin color, jaundice (yellow color in the whites of the eyes from red cell breakdown) (Fig. 6.3), pain in the chest, abdomen, limbs, and joints, slow growth and delayed puberty. Blood transfusions can be used to treat a sudden worsening of SCD resulting from infection or enlargement of the spleen. Acute chest syndrome, when sickle cells block blood flow in the lungs, usually when there is also a lung infection, this can cause chest pain, fluid buildup in the chest, and insufficient oxygen delivered to the body. SCD also affects the complete blood count of the sufferers.

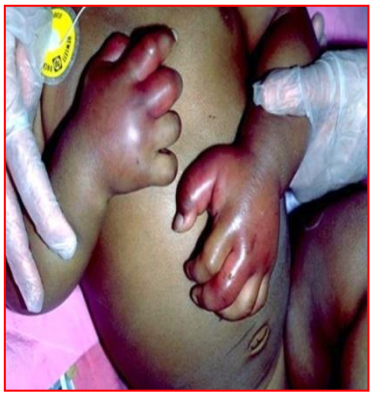

Fig. 6.1: Dactylitis (Hand)

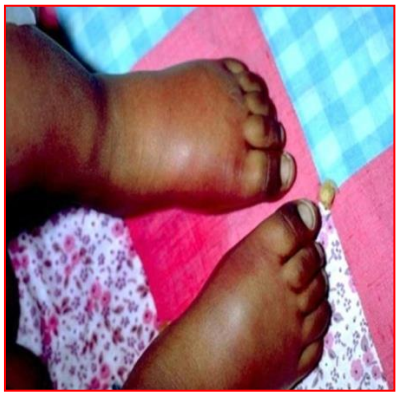

Fig. 6.2: Dactylitis (Foot)

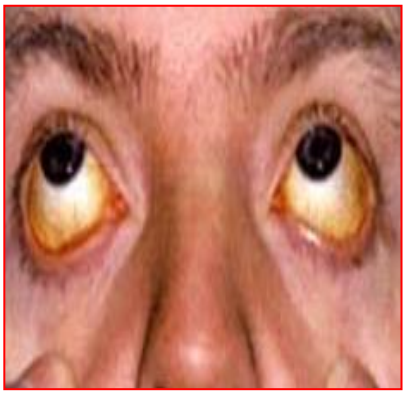

Fig. 6.3: Yellow colored Eyes

Inheritance of SCD:

The disorder is inherited as an autosomal recessive; either two copies of HbS (SS) in the homozygous condition or one copy of HbS (AS) plus another β globin variant (C, D or E) in the heterozygous condition. It is well documented that the gene for sickle cell hemoglobin is located on the short arm of chromosome 11 and has an autosomal recessive inheritance (Lazarus *et al.,* 2011). Hence, it can manifest in two forms viz. heterozygous (carrier) and homozygous (sufferer) (Fig.7). When two carriers marry, the chance of having a homozygous child is 25% with every pregnancy (Kate, 2000). In the homozygous state or sickle cell anemia, affected individuals characteristically are without symptoms until the 2nd half of the first year of life because of sufficient quantity of HbF (α2γ2). Mild hemolytic anemia is apparent by 10- 12 weeks of age, splenomegaly after 6 months of age, first vaso-occlusive episode between 6-12 months by approximately one-half of the subjects, before 6 years by the vast majority. Dactylitis and acute chest syndrome have the highest incidence during the first year of life. The clinical severity is extremely variable, partly due to the effects of inherited modifying factors, such as interaction with β thalassemia or increased

synthesis of HbF and partly to socioeconomic health. Heterozygous state or sickle cell trait is 40-50 times more in number than sickle cell disease. Sickle cell trait is rarely associated with clinical or hematological manifestations of significance.

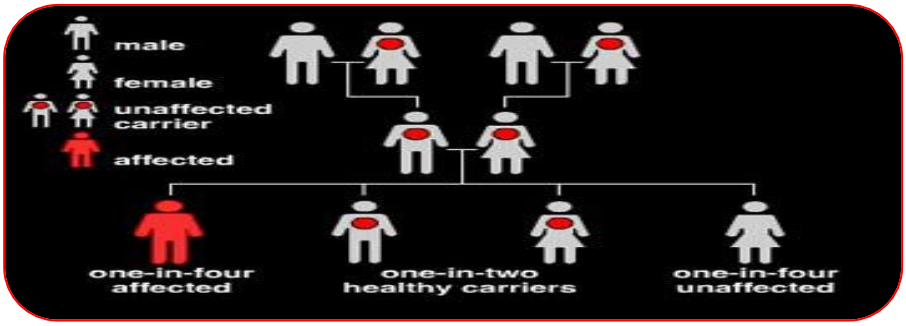

Figure 7: Inheritance of SCD

Recent advances in the management of SCD:

For management of SCD the options were limited but in past few years however, a number of interventions have entered clinical use or are under active investigation.

A. Hydroxyurea

Hydroxyurea is the sole agent proven to have prophylactic value in the treatment of SCD. The drug can reduce the number of vaso-occlusive sickle cell crisis, the number of crises that require hospitalization and the incidence of acute chest syndrome. More recently, data from the large US trial of hydroxyurea suggests that a positive response to the agent lowers mortality from sickle cell disease. A study of hydroxyurea in children suggests that the drug is safe for children as young as five years of age. Further the response rate appears better in children than in adults.

B. Bone Marrow Transplantation

Bone marrow transplantation cures SCD but it need to have an HLA-matched donor which restricts the use of this therapy. Bone marrow transplantation is much more successful in children than in adults. The treatment itself has risks, however, chief among which are immune suppression and graft versus host disease. Bone marrow transplantation using cord blood as a source of hematopoietic stem cells can reduce the incidence of these problems. The limited number of hematopoietic stem cells in cord blood means that the technique can only be used in children. The body mass of adults is too great for marrow reconstitution by relatively few stem cells in cord blood. In vitro stem cell expansion would overcome this barrier.

C. Nitric Oxide

Nitric oxide is a potent signal transducer with aplethora of biological effects. One of the best known of its activities is the relaxation of smooth muscle. A number of trials have been performed, some of which suggest that nitric oxide relieves the pain of acute vaso-occlussive crisis. The fact that nitric oxide is a gas and must be administered by inhalation places restrictions on its use.

D. Gene Therapy

Gene therapy to cure SCD has been slowed by a number of major technical problems. These have included achieving suitably high expression of the hemoglobin A transgene, balanced alpha and beta globin chain expression and adequate infection levels of the hematopoietic stem cell with the viral delivery vehicles. A number of viral vectors have been used including retroviruses and adeno-associated viruses.

E. Gardos Channel Blockers

Cell dehydration contributes to the pathophysiology of SCD. Potassium extrusion through activation of the Gardos channel is a major component of the process. An attempt to block Gardos channel activity using the drug clotrimazole was only partially successful. The blockade of Gardos channel activity was not as great as needed and the drug produced side effects. Newer and more powerful agents that have fewer side effects are now under investigation.

Collaborative Platform for Holistic Management of SCD:

SCD stems from a single codon change in the beta globin gene. This apparently minor alternation ripples through the patient and affects people around the patient, including the family. A comprehensive approach is needed to cope adequately with SCD.

A. The Patient

The patient need more than medication for SCD. Other requirement includes a medical support network that can respond quickly and appropriately in times of need. The complications of SCD are known and sometimes can be prevented by early intervention. Therefore, careful monitoring of potential trouble areas is important. SCD interferes with education and employment. Efforts proving support that minimizes these disruptions are vital. Alternative or non-traditional interventions such as relaxation techniques, self-hypnosis and acupuncture can be very useful. No two patients are identical; so many interventions must be tried.

B. Family

SCD can cripple a family. The disorder might afflict a child, spouse or parent. The effects ripple throughout the whole family. Support must be in place to help the family through difficult times.

Recommendations and Suggestions:

The most serious problem is the sickle cell trait which acts as carrier for propagation of anaemia among the society through consanguineous marriages. Along with this crippling lack of infrastructure, there are many other factors that have aggravated the health crisis in tribal areas like tradition of early marriages and early motherhood, lack of sanitation and clean drinking water facilities and the tribal's blind faith in quacks. All these factors cause overall health crisis of the SS and even AS/AA individuals of the region. Apart from malaria, factors like endogamy, ethnicity and inbreeding are responsible for this variability. Beside the need for care and rehabilitation for the affected patients, effective strategies for control and prevention were recognized as an essential measure toward decreasing the birth of affected children. For a successful control programme, education, counseling and increasing the awareness of chronicity of SCA condition are essential approaches. Government must adopt effective steps directed toward prevention such as (i) community screening and school screening programme (ii) inclusion of relevant information in the school curricula (iii) articles published in newspapers, talk shows on the radio and TV, and (iv) the premarital screening, workshops and symposia and special days for SCD to improve the awareness of the general public and the health care providers. This should be followed by creating awareness, genetic counseling, prenatal diagnosis (if possible) to control the birth of sicklers and the screening for this trait must be encouraged High quality comprehensive care for SCD can be delivered for a low income, aboriginal population in India through a community driven network of care.

Recently, Government of Maharashtra has announced some facilities for SCD individuals which are as follows:

1) Free Blood, medicines, treatment.
2) Free CVS facility
3) Railway ticket concession.
4) Child ICU at Government Medical College Nagpur.
5) Rs 600 per month as financial help for poor.
6) 20 minutes extra time for board exams.

7) Day care center at every District Hospital.
8) Inclusion of Sickle Cell in Bal-Dhoran and Mahila-Dhoran.
9) National Sickle Cell Research Center at Nagpur.
10) Identity Cards to every SCD patient by Government.
11) Sickle Cell Week (11-17 December) every year.
12) Free ST bus travel for treatment.

These facilities for SCD individuals should percolate and reach positively to the people who are in dire need of it.

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CHAPTER
4

INDUCED MUTATION: A PROMISING WAY TO PRODUCE GENETICALLY MODIFIED CROP

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Mutation breeding:

Mutation breeding is one of the conventional breeding methods in plant breeding programme. Transformation breeding is being used for the first time by Hugo de Vries (1903). Transformation breeding has become increasingly popular in recent times as an effective tool for crop improvement (Basu *et al.,* 2008). Mutation techniques are the best method to expand the genetic variability of a species within a short time and have played a significant role in development of many crop varieties. Mutagenesis is used to induce genetic variability in a great number of crops because of some reasons such as – it is simple, relatively cheap to perform, applicable to all plant species and equally useful on small and large scale (Swaminathan, 1995; Siddiqui and Khan, 1999). Essential three phases of mutation breeding are generation of genetic variability, selection of useful genotypes and comparative tests to demonstrate superiority of selected genotypes. Mutation induction is an effective tool for correcting the genetic variation available to plant breeders, especially for traits with extremely low levels of genetic diversity (Szarejko and Forster, 2007).

Induced mutations in crop plants:

Mutations are sudden, permanent, and inherited changes in an organism that are usually structural changes in a gene. It is produced by a change in the original order of the genes and can be spontaneously or artificially induced. Mutation can be induced by using different chemical and physical mutagens. Induced mutation has recently become the subject of biotechnology and molecular investigations leading to explanation of the structure and function of related genes.

Induced mutagenesis has become a proven way to diversify crops. It offers the potential to induce desired traits that are either not found in nature or lost during evolution. When no gene, or gene, for specific disease resistance, or stress tolerance, can be found in the available gene pool, plant breeders have no clear option but to try mutation induction (Singh and Verma, 2015). Induced mutations are generally used for genetic improvement for qualitative and quantitative traits in the plants (Konzak*et al*., 1965,

Sharma *et al.*, 2002). Detailed probabilities and uses of induced change have been compiled and reviewed by Gustafsson (1969), Konzak (1957), Swaminathan (1969, 1972). Mutation breeding Used for the production of many varieties with improved economic value and the study of genetics and plant growth phenomena (Van Der- Bulk *et al*., 1990; Bertagne-Sagnard*et al*., 1996). It has also been shown that mutation can successfully induce genetic variability for many desirable characters and that its practical value is well established in plant improvement programs. The main advantage of mutation breeding is the possibility to modify one or two characters without changing the remaining genotypes. Induced mutations have great potential and serve as a commendable approach to crop genetic improvement (Mahandjiev *et al*., 2001). For the development of new improved crop plants chemical as well as physical mutagenic agents are found to be more beneficial

Mutation breeding:

Micro mutations are important in plant breeding and can be induced artificially with the help of suitable mutagens. Mutagenic treatments increase the genetic variability, which can be used for selection and improvement of plant characteristics. This technique has been used in various plants by Swaminathan (1963), Palenzona (1966) and Scosiroli *et al.* (1966). Mutations employed directly or indirectly for improvement in various traits of plants. In the last century more than one thousand and five hundred direct mutants have been released as varieties. In addition to this, seven hundred mutants have been used in crosses to improved varieties (Laguda, 2004). Induced mutagenesis has been successfully used to generate large variability, particularly for isolating mutants with desirable characters of economic importance such as superior plant types, synchronous maturity, disease resistance, larger seed size and desirable seed colour (Kharkwal *et al.,* 2004).

Mutation induction is an effective tool to improve the genetic variation available to plant breeders, particularly for traits with a very low level of genetic variation (Szarejko and Forster, 2007). It offers the potential to significantly increase crop yields (Kharkwal and Shu, 2009) and induce desired traits, which are either not found in nature or lost during evolution. Treatment with mutagens results in gene alteration or chromosome breakage. Gene mutations occur naturally because of errors in DNA replication but most of these errors are usually not recognized and consequently, genetic variation appears rather limited and breeders have to resort the mutation induction (Adamu and Aliyu, 2007).

Though genetic engineering is becoming a popular tool for crop improvement; induced mutations still carries its significance in terms of simpler infrastructural needs and

its applicability. With the high frequency, certain radiations and chemicals can cause genes mutations that were not possible when only spontaneous mutations were available (Emrani *et al.,* 2011).

Chemical mutagens:

Chemical agents can be useful because they provide high conversion rates and most likely point mutations. The most commonly used chemical mutations for mutation induction belong to the class of alkylating agents [ethyl methanesulfonate (EMS); Diethyl sulfate (DES); Ethylenemine (EI); Ethyl nitroso urethane (ENU), ethyl nitroso urea (ENH), methyl nitroso urea (MNH)] and azides, Sathawane and Khalatkar (1992) successfully demonstrated induction of mutation for low glucosinolate with ethyl methyl sulphonate (EMS), sodium azide (SA) and gamma radiations in *B. juncea*cv.varuna. The tasks of acclimatization and mutant production in the exotic Ethiopian mustard *B.carinata*in to Indian agro climate was effectively carried out by Malode (1995) with the objective to generate new variability, shortening of life cycle, alteration in glucosinolate, erucic acid, oil, protein and fiber content through induced mutations.

Sodium azide (NaN_3):

Nilan *et al.* (1973) used sodium azide as a mutagen in barley for the first time and reported high frequency (17.3%) of chlorophyll mutations at pH=3, a low frequency at pH= 7 and no effect at pH= 11. Sodium azide is a colourless and odourless crystal with molecular weight 65.01 gm. and chemical formula is NaN_3.

Ethyl methyl sulphonate (C_2H_6 OSO $_2$CH $_3$):

EMS, among the chemical mutagens is reported to be the most efficient and powerful mutagen (Minocha and Arnason, 1962, Hajra, 1979). Heslot *et al*. (1959) used EMS, later it is recommended by different scientists as a chemical mutagen. It produces a very high frequency of mutations accompanied by a relatively low frequency of chromosomal aberrations in plants (Froese Gertzen *et al*., 1964; Van Harten, 1998) and at least if one considers the ease of application and the control of after effects (Gaul *et al*., 1972).

Physical mutgens:

Physical mutagens consist of various types of radiation, basically belonging to two different categories. The first series are X-rays and ɣ-rays that generally travel in waves and are related to the electromagnetic spectrum. The second type of radiation involves moving particles, such as protons, neutrons, and electrons, also referred to as corpuscular

radiation (Van Harten, 1998). Mutation induction with radiation is the most widely used method for developing real mutant species, accounting for about 90% of the species obtained (64% with gamma-rays, 22% with X-rays). The types of radiation available for induced mutagenesis applications are ultraviolet radiation (UV) and ionizing radiation (X-rays, gamma-rays, alpha and beta particles, protons and neutrons). Ultraviolet radiation (250–290 nm) has a moderate ability to penetrate tissues when compared to ionizing radiation. Ionizing radiation penetrates deep into tissues and can induce a large number of different chemical changes. The advantages of physical use over chemical mutagenes are the precise dosmetry, which allows for adequate reproducibility and, especially for gamma rays, high and uniform penetration into plant tissues (Jain, 2005).

Physical mutagens:

It has been found that irradiation of seed increases frequency of mutation, promote gene recombination and widen the mutation spectrum (Micke, 1996; Wen and Qu, 1996).

Fruits and ornamental plants are often propagated by mutagenesis. Prediary and Zimmermann (2001) noted that the 6 pier in vitro shoot (Pyrus communis L.) Cultivators were irradiated with gamma rays (3.5 Gyr).

Most mutant species (89%) have been developed worldwide using physical mutagenes (X-rays, gamma rays, thermal and fast neutrons), with gamma rays alone responsible for the development of 60% of mutant species (Kharkwal *et al.,* 2004). During the period 1930-2004, gamma rays were used to develop 64% radiation induced mutant cultures (Ahloowalia *et al.,* 2004). Physiological symptoms in wide range of plants exposed to gamma rays had been studied by many researchers**.**

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CHAPTER
5

GENE DIVERSITY: THE HIDDEN SECRET OF LIFE IN MAN

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Life on our planet displays a stunning array of diversity which istermed as biodiversity. Usually when we think of biological diversity, what first comes to mind are all the different species on Earth interacting with each other, from the very simple bacteria and viruses to other complex multicellular organisms like human. But that's only part of the story. The term biodiversity refers to the biological diversity of life on Earth and therefore that includes multifarious microorganisms, plants, and animals along with their genes and their particularenvironments.It encompasses evolutionary, ecological, behavioural, and cultural aspects.

Trillions of characteristics are hidden in organisms' genomes; the result of all the biological information from thousands of ancestors and millions of years of evolution. All the biological data and variations that make up life on our planet are encoded in DNA. This is known as genetic diversity. Genetic diversity is a major contributor to biodiversity in ecosystems.Genetic studies of the population from the Indian subcontinent are of great interest due to the large population size of India, complex demographic history and unique social structure. Despite recent large-scale efforts to find human genetic diversity, India's vast reservoir of genetic diversity has largely not been discovered. Genetic diversity in species is an important component of biodiversity, playing two important roles at once.

The Indian subcontinent currently has a population of over one billion people belonging to thousands of linguistic and ethnic groups. Conducting genomic research in diverse populations has made significant advances in our understanding of human history, biology, and health disparities, in addition to discovering important clinical significance.The pattern of evolution of Indian population can be visualized from their genetic study. Indian population show regional variation in gene frequencies.Many studies on the Indian population have been put forward to explain their genetic origin and genetic relationship (Bamshad, 1998; Roychowdhury, 2001; Begg, et al. 2004). The genetic relationship between different sex groups is not the same.

Few years ago many anthropologists use the various different morphological characters like body build, facial trait etc as the only source of information use to classify the human population but was found to be changing as per the change in environment and thus failed for the study of genetic history.Subsequently with the discovery of ABO blood group and protein markers and other traditional genetic polymorphisms at the inception of 20th is often thought to mark the beginning of modern study of human variation and relationships. Polymorphism of many genetic traits is now considered as useful tool for differentiation in human population. This is usually done using gene frequency data on the number of genetic locations.

The most common polymorphisms (or genetic differences) in the human genome are single base-pair differences. Scientists call these differences SNPs, for single-nucleotide polymorphisms. When two different haploid genomes are compared, SNPs occur at an average rate of 1,000 per base. Other types of polymorphismsfor example, differences in duplicate number, insertion, deletion, duplication, and rearrangementalso occur, but very rarely.

In 2015, the 1000 Genome Project, which indexed one thousand individuals out of 26 human populations, found that "the general [individual] genome reference differs from the human genome at 4.1 million to 5.0 million sitesaffecting 20 million bases of the sequence"; The latter figure corresponds to 0.6% of the total number of base pairs. By 2017, the Single Nucleotide Polymorphism Database (dbSNP), which lists SNPs and other species, lists 324 million species found in the indexed human genome.The genetic polymorphism in human population in India is greatly study by A. K. Roychoudhury, Bose Institute Kolkata. Pro.ParthaMajumdar group at statistical Institute, Kolkata is pioneered and considered as forerunner in most of the earlier gene diversity studies on Indian population.

Kirk (1976) had studied 10 different population out of which four population are from India (North Indian, Bengali, Marathi) and six population from neighbouring countries (Iranian, Afghan, Sinhalese, Malay, Chinese, Bhutanese) the study was mainly based on the gene frequency data of 10 polymorphic loci (ABO, MN, Rh, Hp, Tf, ACP, AK, 6PGD, PGM-1 and G6PD).

On the other handsanghvi in (1976) had studied 10 polymorphic loci among 3 tribes from south India one form srilanka and one aboriginal each from Malay, New Guinea and Australia. A large number of workers studied the genetic relationship between tribes and

non-tries simply by using the genetic distance data. One of them of Sanghvi in (1953) who was the first to major the genetic distance from five endogamous population in Bombay by using three different loci blood group, PTC, and color vision. Another evolutionary biologist, Roychoudhury studied the genetic relationship by using the gene frequency data of nine polymorphic and four monomorphic loci from seven populations namely Punjabi, North Indian, Marathi, Guajarati, Hindus, Tamils, and Bengalis.

Pandey *et al.* (2003) had studied the dispersal of ABO and Rh blood group, PTC sensitivity and color blindness among seven endogamous populations mainly Tharu, Mushar, Santhal, Dhobi, Kulhaiya and Karan, Kayastha of the Koshi Bihar. Kashyap*et.al* (2003) had studied the genetic variation at 15 microsatellite loci among 54 endogamous groups.

The North Indian Muslim population have great socio-religious, historical and linguistic significance with Indian subcontinent. In (2005) Gene diversity was studied for genetic relationship in some Muslim population of north India by S.S.Arzoo and Mohammad Afzal based on the gene frequencies of ABO, Rh, PTC, and Sickling and G6PD system for six endogamous groups.

In a new study, researchers at the University of Copenhagen and Adelaide have collected and geo-referenced large amounts of genetic data for terrestrial mammals and evaluated long-standing theories that could explain the global distribution of genetic diversity. They found that regions of the world rich in deep evolutionary history, such as the Northern Andes, the Eastern Arc Mountains, the Amazon, the Atlantic jungles of Brazil, the forests of Central America, sub-Saharan Africa and South-East Asia, are also strongholds of genetic diversity. .India is one of the most diverse nation and ranks second in the world after Africa. It is known for its unique range of social, linguistic and biological diversity and thus provides an opportunity to study socio-culture and genetic variability.

Due to the geographical location India has served as a major corridor for the dispersal of modern human out of Africa ~2000000 years ago(Cann,2001) along southern sea routes.

The past two decades have witnessed an explosion of human genetic data. Numerous DNA sequences and genotypes have been generated, and they have led to significant biomedical advances. Furthermore, these data have greatly enhanced our understanding of patterns of genetic diversity between individuals and populations.

For medicine, the study of human genetic variation may be important because certain pathogenic alleles are more frequently found in people of certain geographic regions. New findings show that each human has an average of 60 new mutations compared to their parents.

The purpose of this brief review is to show how our knowledge of genetic diversity can contribute to understanding our similarities and differences, our origins and our evolutionary history.

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CHAPTER

6

BASICS OF IMMUNOLOGY

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Introduction:

Immunology is a branch of biology and medicine that covers the study of immune systemsin all organisms.

Russian biologist Élie Metchnikoff, who first discovered phagocytosis to defend our own body from pathogen coined the term Immunology, and received the Nobel Prize for his work in 1908. His main study work was on starfish larvae, where he demonstrated, small thorns when pierced gets surrounded by some cells.

Immune organs such as spleen, thymus, bone marrow, tonsils, lymph nodes and liver are the major lymphoid organs of the immune system. However, many constituents are circulated in the body in the form of cells. Biopsy of these immune system organs can unveil the illness in fatal situations.

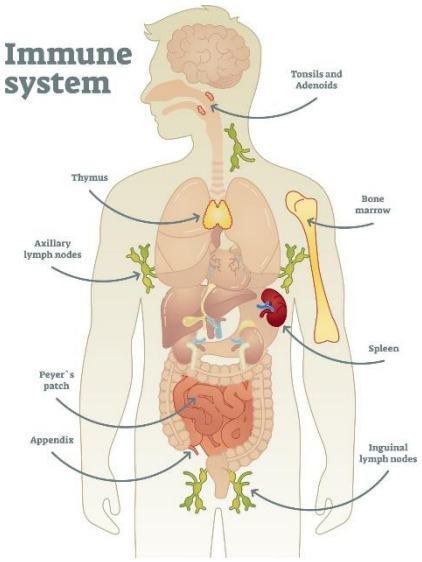

Figure 1: Immune systems organs

The immune system can be differentiated into following two types,

1. The innate immune system – this is preloaded at the time of birth.
2. The adaptive immune system – this immune system defends the body by learning about type of pathogen.

Almost all kinds of animals are born with some kind of protection against pathogens; bacteria being primitive organism still show immunity against viruses.

There are various mechanisms by which immunity in an organism works. Some of the mechanisms are listed below,

1. Phagocytosis
2. Antimicrobial peptides which are called Defensins.
3. Complement system.

Various advanced animals like humans have more sophisticated immune system. Also the ability of adaptive immune system in humans is very much evolved. This capability to memorise patterns of pathogen makes the basis of vaccination.

Innate and adaptive immune system

All the metazoans have innate or pre-acquired immune system only. Whereas more advanced animals like vertebrates has innate and adaptive components.

Basically, inflammatoryand phagocytosis are the modes of responses for innate immune system.

Whereas more advanced immune system type involves lymphatic cells that can distinguish between specific foreign substances in the presence.

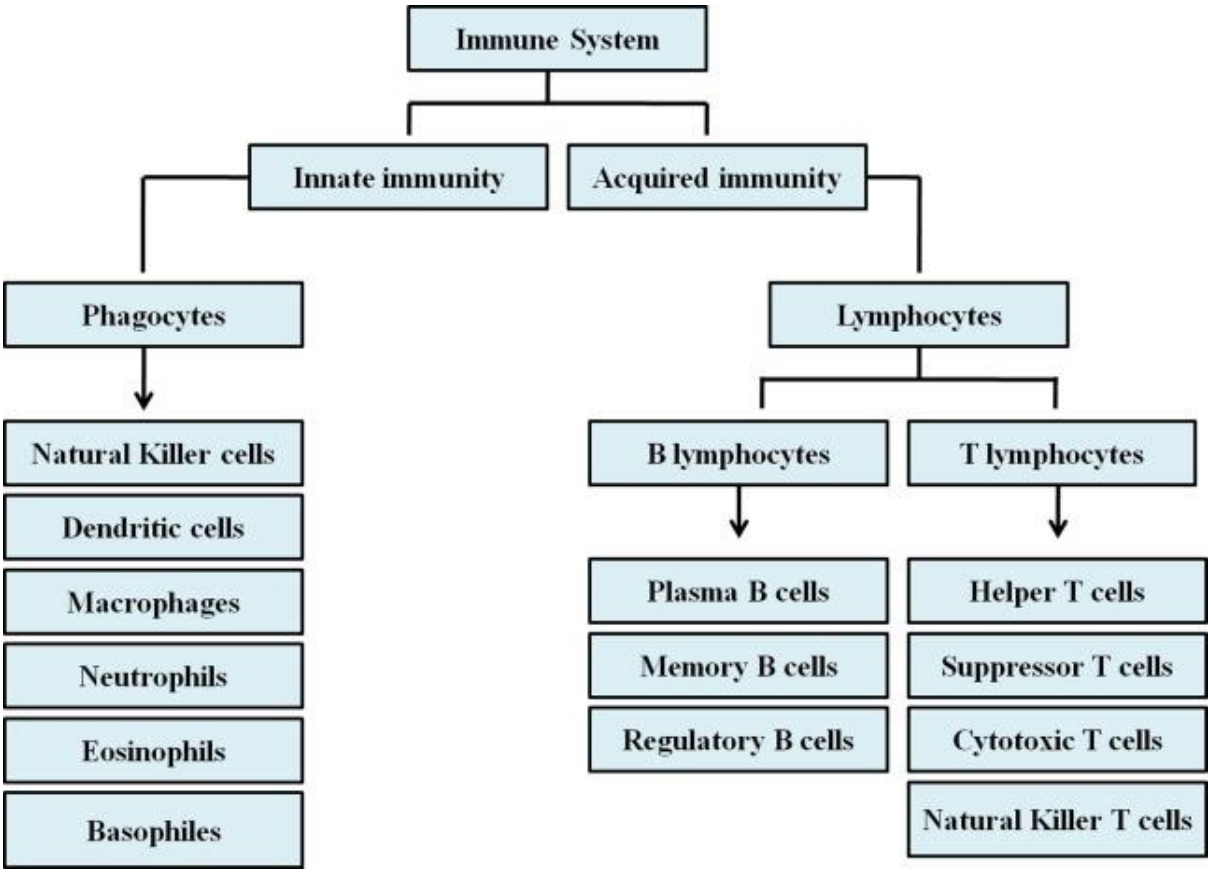

Figure 2: Types of immune system and cells involved

There is equilibrium between recognition of own body cells and foreign particles which gives rise to healthy physical self where only foreign particles are killed sparing surrounding own body cells, when this equilibrium fails the unhealthy state is achieved.

Pre acquired immunity has more non-specific response which is activated at the onset of entry of any pathogen. This response subsequently activates adaptive or acquired immune system which further memorises pathogen pattern once it kills foreign entities.

This field of immunology has been evolved to a great extent, many streams of studies were introduced later, some of the major streams of immunology which are most discussed are listed as follows,

Classical immunology:

Classical immunology is associated with the fields of epidemiology and medicine. It studies the relationship between body systems, pathogens and the immune system. The earliest written mention of immunity is found in the plague of Athens in 430 BCE.

Thucydides noted that people who had recovered from a previous attack of the disease could treat the patient without re-transmitting the disease. There are references to this phenomenon in many other ancient societies, but it was not until the 19th and 20th centuries that the concept evolved into scientific theory.

The study of molecular and cellular components including the immune system, including their function and interaction, is a central science of the immune system. The immune system is further divided into the primitive innate immune system and the spinal cord, the acquired or adaptive immune system. The latter divides into humoral (or antibody) and cell-mediated components. The immune system has the capacity for self and non-self-identification.] Antigen is a substance that stimulates the immune response. The cells involved in identifying the antigen are lymphocytes. Once they are identified, they secrete antibodies. Antibodies are proteins that kill disease-causing microorganisms.

Clinical immunology:

Clinical immunology is the study of diseases caused by disorders of the immune system (failure, dysfunction and malignant growth of cellular elements in the system). It also includes diseases of other systems, where immune responses play a part in pathology and clinical features. Diseases caused by disorders of the immune system are divided into two broad categories:

1. Immunodeficiency, in which parts of the immune system fail to respond adequately (examples include chronic granulomatous disease and primary immune disease);
2. Autoimmune, in which the immune system attacks the body of its own host (examples include systemic lupus erythematosus, arthritis, Hashimoto's disease, and myasthenia gravis).

Developmental immunology:

The body's ability to respond to antigens depends on a person's age, type of antigen, maternal factors, and where the antigen is released. Newborns are said to be in a state of physical immunity, as both their congenital and adaptive immunological reactions are greatly suppressed. Once born, the baby's immune system responds favorably to protein antigens while not to glycoproteins and polysaccharides.

In fact, many infections transmitted by newborns are caused by less virulent organisms, such as Staphylococcus and Pseudomonas. In newborns, the ability to activate optional activity and complementary cascades is very limited. For example, the average C3 level in newborns is about 65% of that seen in adults. Phagocytic activity in newborns is also significantly impaired. This is due to the low optonic activity, as well as the reduced up-regulation of integrin and selectin receptors, which limits the ability of neutrophils to interact with adhesion molecules in the endothelium. Their monocytes are slow and ATP production is reduced, which also limits neonatal phagocytic activity.

Although the total number of lymphocytes is significantly higher than in adults, cellular and humoral immunity is also weakened. Antigen-presenting cells in newborns have less ability to activate T cells. In addition, neonatal T cells proliferate poorly and produce very small amounts of cytokines such as IL-2, IL-4, IL-5, IL-12, and IFN-g that limit their ability to activate the humoral response. Phagocytic activity of macrophages. B cells grow early in pregnancy but are not fully active.

Ecoimmunology and behavioural immunity:

Ecoimmunology, or ecological immunology, explores the relationship between an organism's immune system and its social, biological, and inorganic environment.

More recent ecoimmunological research has focused on host pathogen defense, traditionally considered "non-immunological", such as pathogen avoidance, self-medication, symbiotic-mediated defense, and faculty trade-offs. Behavioral immunity, a line coined by Mark Schiller, specifically refers to drivers who avoid psychological pathogens, such as disgust aroused by stimuli around pathogen-infected individuals, such as the smell of vomit. Monarch butterflies, for example, often lay their eggs on certain poisonous milkweed species when they become infected with the parasite. This toxin reduces parasitic growth in the offspring of infected monarchs. However, when non-infected monarch butterflies are forced to feed only these poisonous plants, they incur fitness costs due to shorter lifespan compared to other non-infected monarch butterflies. This suggests

that laying eggs on poisonous plants is a costly behavior in monarchs that has probably evolved to reduce the severity of parasitic infections.

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CHAPTER
7

RECENT MEDICAL SCIENCE: A BOON BEHIND PANDEMIC

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Abstract:

The COVID-19 epidemic has at the present spread approximately to all parts of the world, leaving a trail of demolition left behind by COVID 19. The virus has by now altered our lives. Several of these changes will have durable implications. Industries in every sector, including Pharma, will require choosing new technologies and new ways of successful working as they familiarize our self to these new realities. Medical technology has approach a extended ways as the inventions. The broader accessibility with associated technology is varying faster than ever before. As per the summary examines on healthcare industry by the World Economic Forum, more than a billion people will need reskilling in medical technology by 2030. In 2020 and 2021, the Covid-19 pandemic mandatory healthcares into the future, and, as a result, numerous encouraging medical technologies were practiced on a huge amount. Now in 2022, we have the same question is how those technologies can be applied together in a post-pandemic world to enhance the pandemic. Hence by this article the attempt was made to aware the peoples about recent medical Sciences.

Keywords: COVID19, Epidemic, Healthcare, Pandemic, Pharma,

Introduction:

The human body is a composite life form and our approach to learn about of composition of Human body is a combining two or more things to form an effective unit or system. We get characterized by the treatment of the intact person, taking into account mental and social factors, rather than just the symptoms of a disease approach in seeing how things can go wrong in the body and how it can be brought back into balance. The first well-known practice perform of medicine is since the Old Kingdom of primordial Egypt, back ago about 2600 BC. Later on, the former recognized code of conduct, the Code of Hammurabi, deal with a lot of aspects of human conduct and, most significantly for our study, established laws governing the practice of medicine.

With the beginning of 2021 promising developments in the technology field are predicted to build a huge impact in healthcare. Starting with artificial intelligence, to 5G capabilities, to robotics, these novel technologies resolve how work is carried out in the healthcare manufacturing and advances the effectiveness by which physicians can make available healthcare services.

Artificial intelligence (AI) offers latest and additional efficient way of life to recognize, analyze, and treat patients. The use of AI may possibly save billions in the healthcare engineering and could improve patient care by civilizing the accuracy of processes. With rising stipulate and growing challenges that treat a superior number of patient's actions, AI can lighten a number of the strains on healthcare personnel. In addition to grow production, AI will support with regulating the use of algorithms in healthcare. AI can aid in the detection of certain diseases, automation of different processes and operations, help on the administrative side of hospitals, and more. These emerging technologies should significantly improve patient care (Marr, 2019). In the future, physicians expect to see about "25 percent of their work being automated" (Park, 2020). Such a large numbers of physicians' workflow could be overtaken by AI, "more than 30 percent of physicians said that they were planning to take classes in AI" (Park, 2020).

Material and Methodology:

Beginning from pregnancy tests to ultrasound scans, medicinal equipment is with us from before our birth. When we feel unwell, diagnostics and checkup policies help healthcare professionals bring back us to good strength as fast as possible.

Recent Medicinal Sciences was built something like the model of operational tests on sick patients to conclude which drug or medical method would best deal with some diseases. This makes Recent Medicinal Sciences more exact in diagnosis and how to treat this specific disease.

A. Effectiveness:

Traditional Medicinal Science treat some diseases but it has never been logically confirmed yet as the way of Traditional Medicinal Science just a sum of information, ability, and practices based on the theories, while recent medicinal Sciences are more successful because the improvement and technique used are more specific in diagnosing diseases and in their treatment with scientifically proved database.

B. Efficiency:

Recent Medical Science determines which drug or medical practice is best deal with illness. This makes Recent Medical Science more precise in determining the diagnosis and how to treat this specific disease. This means Recent Medical Science saves time in treatment as well as in recovery.

C. How to treat and recognize a disease:

Recent Medical Science deal with any disease only as a biological clause characterized by abnormalities in the functioning of definite organs or intact organ systems.

Result:

In 19th century physicians more and more used machinery for analysis or diagnosis. Biomedical Physiology to play a vital role and increases its use in the 19th and 20th centuries to make a diagnosis food, nourishment and diagnosis like diabetes, anemia, diphtheria, and syphilis (Reiser, 1978). In the early hours several of important discovery in medical technology were the thermometer, stethoscope, microscope, ophthalmoscope, laryngoscope, and x-ray. These equipments permitted the general practitioner to perceive sound and observed the various parts of the body that had earlier been examines only in. postmortem studies. Such devices measured to be the first analytical medical acquiring information concerning to the lungs and heartbeats of patients. Initially philosophers challenged its merit and effectiveness of these devices (Reiser, 1978).

Electrical energy resulted in the innovation of the x-ray. Roentgen, a professor of physics in Bavaria, discovered by mistake an emission that could go through solid objects of low density. The discovery of x-rays permitted doctors to view the inside of the body without any surgical procedures (Marks, 1993). Medical Sciences was improving in the 19th century and further then by advances in Biochemistry and pathology techniques and equipment, old ideas about contagious infection spread and control of diseases were replaced with bacteriology and virology.

A recent statement released from the Massachusetts Institute of Technology suggested that that physical sciences have already been changed by their implementation of information technology (IT), advanced materials, imaging, nanotechnology and complicated modeling and recreation. Recent Medical Science suggested pillar like devices, technology, and drugs

A) Devices:

At present there are numerous remarkable medical devices that provide treatment in different conditions and diseases.

Medical devices that come into contact with the human body are essential by the rigid authorities selected and tested on feasible connections and potential discarded unnecessarily side effects. Thus, medical devices are assigned to unusual categories depending on the kind of practice and the contact time to the human body. Medical device are of class I, class IIa /IIb or class III in full conformity with the principles of Good Laboratory Practice (GLP). Collectively associate laboratories.

B) Technology:

Advances in medical Sciences permit us to have access to a number of advantages to facilitate assistance to diagnose and treat various conditions.

i) Remote patient monitoring

In this (RPM) technology general practitioners now able to be acquainted with what is going on with a patient without physically being close. With the help of RPM there are several benefits including improved patient outcomes, quick response time, and considerable expenditure reductions over time. Actually RPM hand in hand with telemedicine in reducing the need for patient travel and alleviate everyone's contact. Governmental changes to Medicare for the Covid-19 pandemic, a variety of forms of RPM were accepted for compensation, efficiently increasing the recognition of this new technology. Surveys say that this practice is fetching so common that found that 88 percent of healthcare providers had invested in or were evaluating adding RPM to their practice

ii) Artificial Intelligence

The main preference use for AI in healthcare 2022 will be into make a use of machine culture to assess huge amounts of patient's statistics and other information. By generating algorithms, technician can copy person's consideration, thoughts and write programs that can apparently imagine, learn, build decisions, and take action. It does mean that, medical care will suddenly shifted to attentive robots. on the other hand, by giving patient's medical records, history, and current symptoms, doctors suggested and diagnoses with treatments plans. Overall with this scrutinized medicinal information's in healthy and ample ways, physicians will be able to use the suggestive data in the form of findings to improve patient outcomes, reduce costs, and boost staff job satisfaction.

iii) Digital therapeutics

Patients suffering from have chronic diseases frequently need constant concern from their Doctors. Which includes patients education, signs monitoring, alteration in prescription, and behavioral changes these all concerns are very costly, band very time-consuming too for both medical workers and patients. To overcome this problem new digital therapeutics plays this role. Using particular software application in Smartphone patient's information about their comfort is reported back to their physician. This way doctors are able to monitor patients exclusive of having to see them repeatedly, over and above spots problems much earlier than when a patient needs to wait for an appointment.

C) Drugs:

It is essential to make a note of that a number of of the best medical innovations have been in the field of drug treatments and therapies.

i) Next Generation of mRNA Vaccine

Advancements in the production, sanitization and cellular delivery of RNA include the improvement of RNA in medical treatments across a large group of applications, such as cancer and Zika virus. This technology is commercial and comparatively simple to produce. in addition during the COVID-19 pandemic it is verified that the world needed rapid production of a vaccine that was easily available around the globe. Because of earlier investigation that laid the base for this technology, a helpful COVID-19 vaccine was developed, accepted and deployed in a year. This useful technology has the possible potential to rapidly and powerfully remove some of healthcare's most difficult diseases.

ii) Plasma Targeted Therapy

Every year more than 200, 0000 peoples are diagnosed with prostate cancer the most frequently diagnosed cancer in the middle of U.S. men. Early on exposure and successful imaging are dangerous for cancer localization, and growth. Prostate-specific membrane antigen (PSMA), found in huge amount on the exterior surface of prostate cancer cells, is a potential biomarker of the disease. PSMA PET uses a radioactive tracer to locate and attach to PSMA proteins, creating them detectable by PET imaging. This approach can be used in combination with CT or MRI scans to investigate where prostate cancer cells to be located in. In 2020, this technology received FDA authorization based on phase 3 trials that showed a substantially increased accurateness for detecting prostate cancer metastases compared to predictable imaging with bone and CT scans.

Conclusion:

The conclusion is that even as effective as Recent Medical Science able to get some characteristic that Ancient Medical Science ignores, this aspect can be important to the accomplishment of the treatment or the wellness of the patient. As World Health Organization confirmed all the way through strict regulations and policies that conventional Traditions and corresponding Medicine (T&CM) can be used along with option to modern medicine. It is not to conclude here which one is better than the other, each has its own advantages and disadvantages. But it is to supplement each other to get the same purpose of well being of mankind.

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CHAPTER

8

ALUMINO-BORATE PHOSPHORS FOR LUMINESCENCE APPLICATION

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Theoretical Background

Introduction

This chapter presents a brief introduction to Luminescence. Theoretical aspects of rare earth (RE) activated alumino-borate based materials, which function as blue emitting phosphors, photoluminescence properties, current trends and innovations in alumino-borate phosphors, limitations and challenges and future prospects and scope of borate phosphors are discussed. This information is crucial in the development of better phosphors in the prospering field of SSL.

Luminescence

Materials exposed to electromagnetic radiation are sometimes important to be able to predict and alter their responses. However, it is not possible until we are familiar with their optical properties and understand the mechanisms responsible for their optical behaviors. When a solid absorbs photons or charged particles, a number of energy conversion processes are possible, as illustrated in fig. 1. These include luminescence (photon emission), electron emission, thermal emission, and chemical/structural change. Luminescent materials, also known as phosphors, can absorb energy from the incident radiation and emit light after a series of energy transfer processes. The word phosphor comes from Greek language and it was considered as “light bearer”. Luminescence is referred as an old technique. First observed in an extract of Lignum nephriticum by Monardes in 1565, it took until 1852 to be fully described by Sir G. G. Stokes who reported the theoretical basis for the mechanism of absorption (excitation) and emission. Today luminescence, in its varied forms, is one of the fastest growing and most useful analytical techniques in science. Applications can be found in areas as diverse as materials science, environmental science, microelectronics, physics, chemistry, biology, biochemistry, medicine, pharmaceutical science, toxicology and clinical chemistry. This rapid growth has occurred only in the past couple of decades and has been principally driven by the unique needs of the life sciences (DeLuca, 1980).

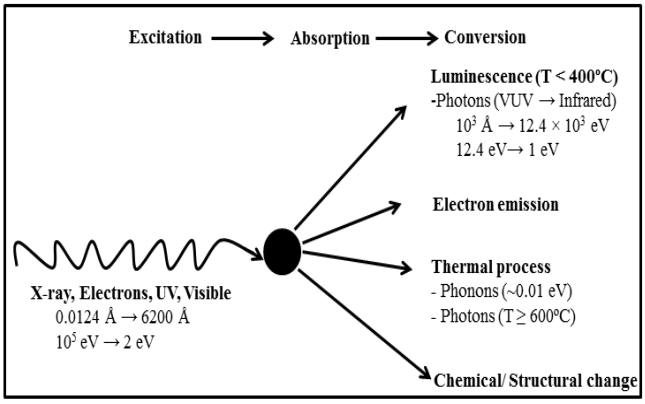

Figure 1: Conversion of primary excitation energy in solids

Luminescence Mechanisms

Luminescence can also be divided into phosphorescence and fluorescence by the difference in decay time. The term fluorescence and phosphorescence are usually referred as photoluminescence because both are alike in excitation brought by absorption of a photon. Fluorescence differs from phosphorescence in that the electronic energy transition that is responsible for fluorescence does not change in electron spin, which results in short-live electrons (<10-5 s) in the excited state of fluorescence. In phosphorescence, slow photoluminescence occurs in this process. In contrast to Fluorescence, it demonstrates itself as a glowing that lasts long after the excitation light is gone. As there is a change in electron spin, which results in a longer lifetime of the excited state (second to minutes). Fluorescence and phosphorescence occurs at longer wavelength than the excitation radiation (Blasse and Grabmaier, 1994).

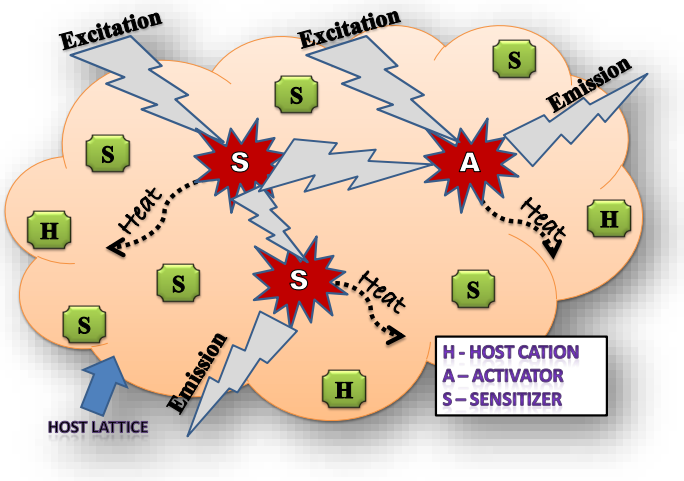

Figure 2: Luminescent material containing activator ions A (ions showing the desired emission) and sensitizing ions S (on which, e.g., UV excitation can take place)

Photoluminescence

Photoluminescence in the ultraviolet-visible comprises of two similar phenomena: fluorescence and phosphorescence. In the process of luminescence, when radiation is incident on a material some of its energy is absorbed and re-emitted as a light of a longer wavelength (Stokes law). The wavelength of light emitted is characteristic of a luminescent substance and not of the incident radiation. The light emitted could either be visible light, ultra-violet, or an infrared light. This cold emission, i.e. luminescence, that does not include the emission of blackbody radiation, involves two steps: (1) The excitation of electronic system of a solid material to higher energy state, and (2) subsequent emission of photons or simply light. The emission of light takes place at characteristics time 'τ_c' after absorption of the radiation.

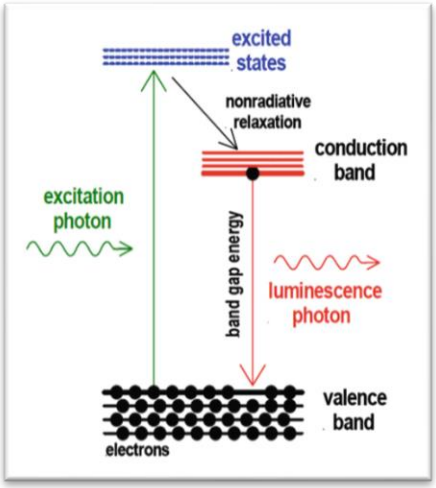

Figure 3: Radiative and non-radiative processes that can occur during photoluminescence mechanism

Luminescent properties of rare earth ions

The history of the rare earth elements (also called lanthanides) started almost 220 years ago in 1788 when Geijer reported on a black stone found close to the Swedish town of Ytterby. The stone was called Yttria (Bachmann, 2007). When RE ions placed in a crystal lattice, it is subject to a number of forces, which are, absent in the free ion. Inorganic solids doped with different RE impurities are used in display application. It is necessary to understand the mechanism of these display materials. The characteristic properties of the RE ions are attributable to the presence in the ion of a deep-lying 4f shell, which is not entirely filled (Kim *et al.,* 2001). In solids, the emission of RE ions is observed at different spectral position than the absorption. The difference between the absorption and emission

wavelength is described as 'Stokes Shift' (Ko, 2003). Rare-earth doped luminescent materials are extensively used in the lighting industry (Li, 2005; Bunzli *et al.,* 2007; Li *et al.,* 2007; Ji *et al.,* 2010; Naik *et al.,* 2015) as well as plasma display panel (PDP) technologies (Kharabe *et al.,* 2014).

Table 1 presents the number of 4f electrons and the radius of the R3+ ion for the rare-earth elements (Castor and Hendrick, 2017; Pecharsky and Gschneidner, 2017). Depending on the rare earth ions, the luminescence spectra can be divided into two types: broad band and sharp lines. Each group of sharp lines corresponds to an electronic transition between an excited state and a ground state designated by the total angular momentum, J, and it can be properly assigned by employing the Dieke diagram (Xie *et al.,* 2011).

Table 1: The number of 4f electrons and the radius of the R^{3+}ion for the rare-earth elements

Rare earth Element	symbol	Atomic number	Number of 4f electrons	Number of unpaired 4f electrons	ionic radius (Å)
Lanthanum	La	57	0	0	1.045
Cerium	Ce	58	1	1	1.010
Praseodymium	Pr	59	2	2	0.997
Neodymium	Nd	60	3	3	0.983
Promethium	Pm	61	4	4	0.970
Samarium	Sm	62	5	5	0.958
Europium	Eu	63	6	6	0.947
Gadolinium	Gd	64	7	7	0.938
Terbium	Tb	65	8	6	0.923
Dysprosium	Dy	66	9	5	0.912
Holmium	Ho	67	10	4	0.901
Erbium	Er	68	11	3	0.890
Thulium	Tm	69	12	2	0.880
Ytterbium	Yb	70	13	1	0.868
Lutetium	Lu	71	14	0	0.861
Scandium	Sc	21	0	0	0.745
Yttrium	Y	0	0	0	0.900

Borates Phosphors

Since the 1930s, when the first borate crystal structures were determined at ambient conditions by Zachariasen, Goldschmidt, Hauptmann and others, more than 2500 (re-)determined crystal structures of hydrous and anhydrous borates have been listed in the ICSD Database (ICSD-2016) up to now. Modern descriptors of borate rigid groups, fundamental building blocks (FBBs) and finite clusters were introduced. The nomenclature of crystal structures and several classifications of borates have been described in a large number of review papers. As a result, the basic crystal chemistry principles of borates were established:

(1) Boron atoms do occur equiprobably in both triangular and tetrahedral coordination to oxygen atoms and hydroxyl groups in the structures of crystals and glasses.

(2) The BO3 triangles or/and the BO4 tetrahedra are connected via common corners (oxygen atoms) to form rigid cyclic 3B-groups composed from three of such polyhedra; several such groups can also be linked via shared BO4 tetrahedra, thus forming multiple cyclic rigid groups. BO4 tetrahedra scarcely share edges. These ways of condensation lead to the formation of boron–oxygen entities that do not change significantly in various crystals and glasses.

(3) The rigid groups or their combinations linked by shared oxygen atoms constitute the fundamental building blocks (FBB) of the structure (Bubnova *et al.,* 2017).

Due to interesting chemical and physical properties exhibited by inorganic solid state borate materials, these materials become centre of attention for the material scientists. Borates form a great number of compounds having diverse structures due to three-fold or four-fold coordination of borate atoms. Borates intrinsically possess characteristics that are advantageous for optical materials, which include wide transparency range, large electronic band gap, good thermal and chemical stability, low preparative temperature, optical stability with good nonlinear characteristics and exceptionally high optical damage threshold. The unique crystal structure of borates determines their enhanced UV transparency, good nonlinearity and relatively high resistance against laser induced damage. Borate compounds are very good hosts for development of luminescent materials. Variety of borate host materials doped with rare earth and other ions have been reported as phosphor materials for variety of applications (Palaspagar *et al.,* 2015). In this study BaB_8O_{13} and $LiBaBO_3$ borate phosphor powders were studied.

Alumino-Borates Based Phosphors

A great interest in phosphors has resulted in rapid developments in the promising display and illumination technologies (Kharabe *et al.,* 2014). For general lighting applications such as in UV LEDs, various photoluminescent materials including different classes such as oxides, silicates, aluminates, alumino-borates, alumino-silicates, nitrides, borates, etc., play vital roles. Among all these hosts studied, borate phosphors are proved to be good candidates due to their advantages like low synthetic temperature, easy preparation, and high luminescent brightness. However, compounds belonging to alumino-borate family now a day seem to be promising for high luminescent efficiency and good thermal stability (Ronda, 1997; Kang *et al.,* 1998; Hong *et al.,* 2000; Lun *et al.,* 2001). Rare earth doped alumino-borate compounds have high UV transparency and exceptional optical damage threshold, which makes them attractive for numerous practical applications such as, in lamps and display applications. There are many excellent phosphors in the borate family, for example, $CaAl_2B_2O_7$: Eu^{2+}, $BaAl_2B_2O_7$:Ce^{3+}/Tb^{3+}, $Al_3GdB_4O_{12}$:Eu^{3+} and $SrAl_2B_2O_7$:Eu^{3+}, etc. which has been applied in the region of UV-excited phosphors and integrated optics (Zhang and Li, 2004). Rare earth borate compounds are an interesting class of luminescent materials.

Current trends and Innovations:

The need of new materials with desirable optical properties has become important issue in the recent year. In particular, need has emerged for compounds having better luminescent properties in various practical applications. From the literature survey, it is clear that the luminescence properties of the compounds depends largely on the physical properties such as, particle size, morphology, particle distribution, surface area and state of agglomeration. Introduction of rare earth ions as activators improves the luminescence properties of the compounds considerably.

Luminescence continues to play a major technological role for mankind. However, solid state luminescence is now set to significantly displace gas discharge luminescence in many areas, in much the same way as gas discharges have already displaced tungsten filament incandescence. Therefore, the high conversion efficiencies now demonstrated for inorganic light-emitting diodes. Although there are a variety of ways of exciting luminescence materials, all forms of luminescence are generated by means of accelerating charges. With increasing concerns about energy savings, environmental protection, and life quality, novel lighting sources that exhibit higher luminous efficacy, energy efficiency, and longevity are continuously pursued. However, SSL is a new lighting source that is based on

semiconductor devices, with the light emitted by solid-state electroluminescence, which has great potential to significantly surpass the energy efficiencies of incandescent and fluorescent lamps, and thus promises huge energy savings and reduction of greenhouse gas emissions (Xie *et al.,* 2011).

Limitations and Challenges

In addition, as compared to other compound phosphor materials, alumino-borates based phosphors have an exceptional optical damage threshold, able to withstand the harsh conditions in vacuum discharge lamps or screens (Corbel *et al.,* 1998; Cheng *et al.,* 2000; Cui *et al.,* 2006) reover most of the UV excited alumino-borate phosphors reported in the literature were prepared by either conventional solid state high temperature method (SSD), or in some other cases citric sol-gel (CSG), spray pyrolysis, co-precipitation, and combinatorial chemistry approach has been employed. SSD method has many technical disadvantages, such as, this method consumes much energy during preparation and the coarser grain size of phosphor powders prepared by this method is in the range of 10 to 20 microns and the particle size distribution is not uniform, making the quality of coating low. The high temperature method, sophisticated synthesis techniques and the use of costly chemicals increase the cost of phosphors and displays device. Therefore, there is need of improvement via various aspects such as physical, chemical and luminescent properties in alumino-borate based materials so that it would be useful as commercial phosphors by removing or modifying all the drawbacks. With the expectation of improvement in physical, chemical and luminescent properties of RGB emitting alumino-borate based phosphor.

Future Prospects and scope

Exploratory research in solid state luminescence plays an important role in the discovery of new materials with enhanced optical performance. Alkali/Alkaline alumino-borates are a part of those materials of interest that have drawn particular attention due to their diverse properties of technological importance. Traditionally, most of the alumino-borate phosphors were synthesized by solid state technique required very high temperature. However, we anticipate some good results to come if these alumino-borate phosphors doped with different rare earth ions synthesized by adopting low cost low temperature and time saving solution combustion technique.

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CHAPTER
9

A GREEN SYNTHETIC APPROACH FOR THE DOPED ZnO NANOPARTICLES FOR OPTOELECTRONIC APPLICATION

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Theoretical Background

Green synthetic approach for ZnO

Nanostructures of metal and semiconductors hybrids have gained significant interest in recent years due to their potential applications in the emerging fields of nanotechnology (Sun *et al.,* 2009). Size, shape, surface area, inertness and conductivity are few parameters of selecting these materials. Among many materials, Zinc oxide (ZnO) nanostructures have proven to be a suitable candidate for various applications due to its superior characteristics; which include wideband gap (3.37 eV), large excitation binding energy (60 meV) and high electron mobility (about 115–155 cm2/V/S) (Das, *et al.,* 2017). ZnO is a unique and versatile material that exhibits both semiconducting and piezoelectric properties also having high interfacial area, which allows more electron–hole formation in presence of UV light, essential criteria for optoelectronic devices (Singh, 2010). Other favorable aspects of ZnO include its non-toxicity, biocompatibility, low cost, easy synthesis with varying morphology (nanorods, nanoflowers), andlow power threshold (Xia *et al.,* 2016). Together, these properties makes ZnO an ideal candidate for a variety of applications in solar cells, gas sensors, photo catalytic, antibacterial, electrical and optical devices (Rekha *et al.,* 2010). Recent studies show ZnO nanostructure has potentialas antibacterial agents in lotions, mouthwashes, ointments, and microbial efficacy against growth. Moreover, there have been significant efforts underway for the development of UV photodetectors, UV lasers, and switches using ZnO nanostructures (Maiti *et al.,* 2015). The green synthesis of nanoparticles is a good substitute for physical and chemical methods. Various synthetic parameters use for the ZnO materials itself is a versatile application. The synthetic methods comprises of sol-gel combustion, chemical vapor deposition, sonochemical, hydrothermal, wet polymerization, solvothermal, thermal decomposition, microwave assisted, precipitation, micro-emulsion, lyophilization and laser ablation (Kaviyarasu *et al.,* 2016a, 2016b). The green synthetic method, employing biological plant extracts is one of the more extensively acknowledged routine due to its several advantages,

which requires no additional chemicals, simple, environmental friendly, inexpensive and reliable method (Thema *et al.,* 2016).

Nanoparticles an emerging stream

Nanomaterials have been called 'a wonder of modern medicine' and elicited much interest over the past few decades (Gunalana *et al.,* 2012). Nanomaterials are of great importance because of their superior physicochemical and biological properties over their bulk phase. The size of these nanostructured materials (1–100 nm) offers a higher surface to volume ratio, which led to high surface reactivity (Geonmonond *et al.,* 2018). This distinct property allowed them to be utilized in vast applications in many fields ranging from material science to biotechnology. The synthesis of nanostructured materials is without question the most important and powerful technique for fabricating nanosized semiconductor devices, and applications of the technique and knowledge made many of the most important scientific advances emerged in the twentieth century (Sue *et al.*, 2019). Nanostructures of metal and semiconductors hybrids have gained significant interest in recent years due to their potential applications in the emerging fields of nanotechnology (Sun *et al.*, 2009).

ZnO Nanoparticles

Among those, ZnO NPs are used in the elimination of toxic chemicals like arsenic, sulfur from water sources owing to their large surface area by volume ratio than the bulk materials (Khan *et al.*, 2016). Zinc oxide has remarkable application in micro- electronics, diagnostics, optoelectronic devices, biomolecular detection, surface acoustic wave devices like laser devices, electromagnetic coupled sensor. They can act as an alternative source for degradation of atmospheric pollutants (Mirzaei and Darroudi, 2017).

ZnO is a member of the group II–VI semiconductors family, whose covalence is on the boundary between ionic and covalent semiconductors. ZnO is a stable material with melting temperature of the order of 2248 K, making it withstanding high temperature treatments associated with doping and forming ohmic contacts. The ZnO has a intrinsic properties with broad range of radiation absorption, high photostability and large electrochemical coupling coefficients which makes it a good choice for short wavelength optoelectronic and photonic devices (Chaari and Matoussi, 2012; Ludi and Niederberger, 2013).

Various Synthetic approaches for ZnO nanoparticles

Due to the increasing popularity of green methods, different works had been done to synthesize ZnO NPs using different sources like bacteria, fungus, algae, plants and others. Plant parts like leaf, stem, root, fruit, and seed have been used for ZnO NPs synthesis because of the exclusive phytochemicals that they produce. Using natural extracts of plant parts is a very eco- friendly, cheap process and it does not involve usage of any intermediate base groups (Agarwal, *et al.*, 2017). NP synthesis using bacteria is a green approach but it has several disadvantages like screening of microbes is a time-consuming process, careful monitoring of culture broth and the entire process is required to avoid the contamination, lack of control on NP size, shape and cost associated with the media used to grow bacteria is also very high. Algae have been used extensively for the synthesis of Au and Ag nanoparticles but its application for the ZnO nanoparticle synthesis is limited and reported in very less number of papers. Microalgae draw special attention because of its ability to degrade toxic metals and convert them to less toxic forms (Thema *et al.,* 2015).

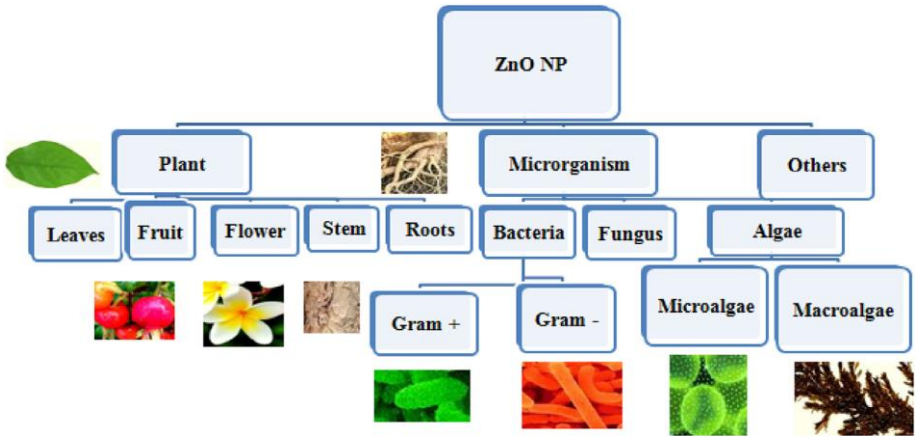

Figure 1: Different green synthetic approaches for ZnO

Significance of the study in context of current status

The decrease in ZnO particle size at nanoscale causes a rise in the surface-to-volume ratio. Previously, conditions on the surface of ZnO NPs were altered by incorporating dopants; their photocatalytic behaviour was momentously boosted (Damonte *et al.*, 2009; Xiao and Ouyang, 2009). The doping of rare earth elements in ZnO significantly improves the properties of ZnO NPs. Rare earth elements play a significant role in various innovative technologies such as photocatalytic and luminescent fuel cells. Rare earth elements are valuable additives to metal oxide due to their 4f–5d and 4f–4f electronic transitions, which are unlike those of other elements (Carreno *et al.*, 2004; Lucovsky and Phillips, 2005). The photocatalytic activity of ZnO is improved by varying the size and shape of ZnO

nanoparticles (Holkar *et al.*, 2016) and surface of ZnO nanoparticles can be modified by deposing metal materials on them to form heterostructures at the interface, thereby creating a nanocomposite. The chemical and physical properties (luminescent and electro-optic chattels) of the host material are modified by doping the metals or metal oxides; these have various potential applications (Faraz *et al.*, 2018).

Future prospects and scope

Despite the numerous applications, exposure to ZnO NPs poses a significant threat to human health and the ecosystem. Though ZnO NPs offer significant safety and biocompatibility, their unregulated and uncontrolled use may have intended consequences for the biological system. Considering the future potential of ZnO NPs, it is unavoidably necessary to have a better grasp of their toxicity. It is also believed that ZnO NPs would significantly advance medical progress and are predicted to make even more intriguing contributions in these domains. Although ZnO NPs have shown exceptional promise inthe diagnosis and treatment of cancers, more in-depth and advanced analysis of ZnO NPs, detailed understanding of the cellular and molecular pathways, and clinical trials will berequired in the future for better cancer theranostic.

Zinc oxidehas shown excellent effectiveness in controlling various other properties of foodmaterials such as solubility, moisture absorption, monolayer moisture, and also physical properties including tensile strength, permeability, and degree elongation of foodas well as edible packaging materials. ZnO-NMs have potential scope of application inagriculture, food processing, quality and safety assurance, preservation, and packaging. Till date along with other sectors of food processing, its commercial application infood packaging is more prominent and rapidly expanding. However, additionalresearch is still needed to understand and establish the toxicological effects of ZnONMs, in order to assess their long-term and short-term impact on consumers. Inaddition, there is a challenge to explore other interdisciplinary domains for theapplications of ZnO-NMs to solve various existing problems of society.

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CHAPTER
10

FOURTH GENERATION POLYMER SOLAR CELLS

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Abstract:

Greenhouse gases and their damaging effects on the atmosphere have received increased attention following the release of scientific data by United Nations Environment Programme and World Meteorological Organization that show carbon dioxide to be the main contributor to increased global warming. The solution of this problem lies in generation of energy from natural sources. Alternative energy refers to energy sources that have no undesired consequences such for example fossil fuels or nuclear energy. Alternative energy sources are renewable and are thought to be clean energy sources.This work briefly reports the recent developments in fourth generation solar cell. In addition to this, present work listed the major challenges associated with fourth generation solar cell technology are also discussed.

Keywords: Conducting Polymer; Solar Cell, Low Cost

Introduction:

Energy is very crucial parameter for development of any nation and now a days most of the nation fulfilling their need of energy from the diminishing fossil fuel. The burning of fossil fuel to responsible to the global warming and climatechange. Therefore, clean energy production is the ultimate option for sustainable growth. Considering the urgent need, researchers across the globe focusing on the developments of efficient photovoltaic materials.

In last 5 decades, photovoltaic technology has undergone through numerous upgradations. The pictorial representation of different generation of solar cells depicted in Figure 1. On the basis of upgradations, till date the PV cells are classified under 4 different generation,

1st generation: Mono Crystalline Silicon; Polycrystalline Silicon

2nd Generation: Hydrogenated amorphous silicon; CdTe Thin Film

3rd Generation: Nanocrystal; Polymer based; Perovskite; Dye Sensitized Solar cell

4th Generation: Hybrid Solar Cells

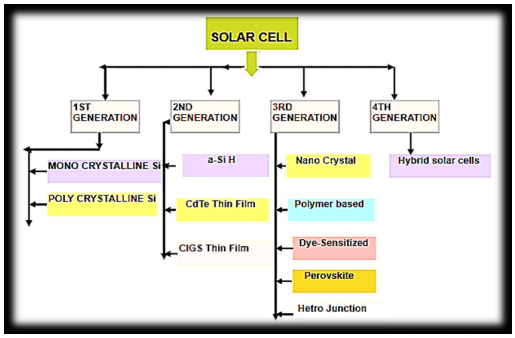

Figure 1: Generation of solar cells (Tripathi, 2019)

Fourth generation solar cells are prepared using the combination of low-cost polymer and inorganic nanostructure. Literature study shows that such combinations are give considerable results by providing significant power conversion efficiency and stability. The fabrication process of this type of PV cell is simple and less expensive than previous generations with outstanding features such as high energy harvesting cross-sections, the charge dissociation, andcharge transport within the PV cells.

Review of literature:

In this section, the literature survey of polyaniline based photovoltaic materials is presented. Yu et al studied the photovoltaic performance of polyaniline (PANi/MPt, M = Mo, Pd, Co) counter electrodes prepared by an electrochemical deposition technique. The results of the study show that PANi/CoPt, PANi/PdPt, and PANi/MoPt counter electrodes systems have power conversion efficiency of the order of 8.08%, 7.26% and 6.83%, respectively (Yu *et al.,* 2016).

Wang *et al.* (2008) employed a hole conducting polyaniline (PANi) layer to fabricate amorphous silicon/polyaniline n–i–p heterojunction solar cells. They used spin-casting method by differing polyaniline dispersions corresponding to film conductivities ranging from 10^2 to 10^2 S/m and observed open-circuit voltages (V_{OC}) in 0.5–0.7 V range. Their work highlights the limiting mechanism caused by electrophoresis effects in the PANi.

Ameen *et al.* (2009) used aniline monomer to prepare TiO2/polyaniline (PANi) and dye absorbed TiO_2/polyaniline electrodes by plasma enhanced polymerization for the fabrication of dye-sensitized solar cells, observed that TiO_2 greatly improves electrical conductivity of pristine PANi and achieved the overall conversion efficiency of ~0.68%. Their study reveals that the dye absorbed TiO_2/PANi electrode based DSSCs might cause the high charge carrier transportation between the TiO_2 and the PANi layer which improves the conversion efficiency as compared to the TiO_2/PANi electrode.

Shen *et al.* (2008) prepared nano-crystalline titanium dioxide films by sol–gel spin-coating method and made sandwich structure polymer solar cell of indium-tin oxide (ITO)/nano-crystalline TiO_2/polyaniline/Al. TiO_2 sol is prepared by varying the ratio of titanium alkoxide and ethanol. For the ratio of titanium alkoxide and ethanol at 3:7, they achieved largest open voltage (Voc) of 0.397V and short current density (Jsc) of 65.9μA/cm^2 under simulated solar radiation. I–V characteristics of prepared cell indicate that a p–n junction is formed at nano-crystalline TiO_2/polyaniline interface and so junction shows rectifying behavior.

Chen *et al.* (2010) have prepared dye-sensitized solar cell (DSSC) using 1-propyl-3-methylimidazolium iodide (PMII). Polyaniline-loaded carbon black is used as the composite electrolyte which is placed in between TiO_2 electrode and platinum counter electrode. In this experiment, one DSSC is fabricated using electrolyte without added iodine which achieves power conversion efficiency of 5.81% and other DSSC is fabricated with the addition of low-viscosity binary ionic liquid (bi-IL) of 1-ethyl-3-methylimidazolium thiocyanate which achieves power conversion efficiency of 6.15%. When compared at room temperature even after 1000 hrs the power conversion efficiency of quasi solid-state DSSC with bi-IL shows a decrease of hardly 3% compared with that of a liquid electrolyte DSSC which shows a decrease of about 30%. In this work, a low cost DSSC using the bi-IL is also fabricated which have the polymer layered counter electrode prepared through electrodeposition technique and it shows an efficiency of 5.27%.

Ebrahim *et al.* (2010) used Copper indium disulfide ($CuInS_2$) to fabricate florin doped tin oxide (FTO)/$CuInS_2$/ polyaniline base/ZnO/FTO hetrojunction solar cell, as $CuInS_2$ has good photovoltaic conversion efficiency due to direct band-gap energy of about 1.5 eV and a large absorption coefficient. By electrodeposition technique $CuInS_2$ thin films were electrodeposited onto fluorine doped tin oxide substrate. Short circuit current, open circuit voltage, and efficiency is observed for FTO/$CuInS_2$/ZnO/ITO herterojunction solar cell and FTO/$CuInS_2$/polyaniline base ZnO/ITO herterojunction solar cell which are 3.2×10^{-6} A/cm^2, 0.714 V, 1.92×10^{-3} % and 3.25×10^{-6} A/cm^2, 0.724 V, 1.8×10^{-3} % respectively.

Yang *et al.* (2011) grafted aniline on aminobenzoate monolayer that is chemically adsorbed on the TiO_2 nanocrystal surface to fabricate a uniform core/shell structured TiO_2/polyaniline nanocomposite. FT-IR, UV–Vis spectra, TEM, FE-SEM, and TG–DTA analysis techniques are used to investigate this nanocomposite's characteristics and formation. The study shows that in a photoelectrochemical reaction this nanocomposite

acts as a visible-light sensitizer and a dye-sensitized solar cell fabricated with a sensitized electrode of TiO_2/polyaniline film gives short circuit current density of 0.19 mA/cm^2 and an open circuit voltage of 0.35 V.

Joshi *et al.* (2012) obtained multilayer thin film heterojunction of ITO/CdS/Polymer/$CuInSe_2$/Ag by sandwiching the conjugated conducting polymer in n and p-type wide band gap semiconducting material, on the ITO coated glass substrate by multilayer chemical deposition method. The heterojunction solar cell was examined for structural, compositional, optical and solar cell characteristics under 100 mW/cm^2 of illumination. The result of impinging conjugated polymer (polyaniline) in nanostructured CdS/CuInSe2 heterojunction thin film solar cell results in increase in conversion efficiency from 0.26% in CdS/CuInSe2 to 0.55% in CdS/Polymer/$CuInSe_2$ upon illumination which was shown by I-V analysis. Wang *et al.* (2012) synthesized a graphene/polyaniline nanocomposite carried out polymerization of aniline monomer by *in situ* method, under acid condition in the presence of graphene sheets. In a dye sensitized solar cell, the prepared graphene/polyaniline nanocomposite deposited on fluorine-doped tin oxide glass was used as counter electrode which resulted in conversion efficiency of 6.09% compared to 6.88% of efficiency for the cell with expensive Pt counter electrode under similar experimental conditions. Zhu *et al.* (2012) prepared polyaniline (PANi) hybridized ZnO photoanode by two-step process: hydrothermally growing ZnOnanograss on the fluorine-doped tin oxide (FTO) substrate and then polyaniline is chemisorped on the surfaces of the ZnO nanorods. The surface morphology and the structure ofPANi and ZnO in the PANi hybridized ZnOnanograss films were studied by scanning electron microscope, X-ray diffraction and Fourier transform infrared spectra techniques. Pure ZnOnanograss as well as PANI hybridized ZnOnanograss were applied to DSSC and comparative results of photoelectrochemical measurement shows that PANi hybridized ZnOnanograss photoanode increases the overall light-conversion efficiency by 60% than that of a pure ZnOnanograss photoanode. The electrochemical impedance spectra (EIS) shows that there are larger electron densities in photoanodes of PANi hybridized ZnOnanograss than that in pure ZnOnanograss and so dye-sensitized solar cell with PANi hybridized ZnOnanograss films performance better.

Challenges:

During the study of fourth generation PV cell following challenges are still present,

1. Concentration optimization in polymer matrix is still challenging task for researchers.

2. Materials used in fourth generation PV cell are not robust against the atmospheric changes.

3. Fourth generation PV cellare less stable than previous generation PV cell.

Conclusions:

In the light of above discussion, it is observed that generation PV cell technology is in primary stage. Many parameters such as concentration optimization in polymer matrix, robustness against the atmospheric changes and stability are remains to improve. But good power conversion efficiency and fill factor motivate researchers to put their efforts to improve robust against the atmospheric changes.

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CHAPTER
11

RECENT ADVANCES IN TIO_2 BASED NANOFIBERS

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Abstract:
This paper reports the review on recent advances in the modification of TiO_2 based nanofibers. The TiO_2 based nanofibers are prepared using various composition and characterized through different techniques such as scanning electron microscopy (SEM) andhigh-resolution transmission electron microscopy (HRTEM) to study surface morphology, UV-vis (Ultraviolet-Visible) spectrophotometer to examine the UV-vis absorption spectra, thermal gravimetry analysis (TGA) and differential thermal analysis (DTA) to investigate thermal properties, X-ray diffractometry (XRD) was done to study phase analysis, Raman spectroscopy, X-ray photoelectron spectroscopy (XPS) done to determine the diameters and average surface pore sizes of the electrospun nanofibers. Also, as-synthesized materials have potential application in electronic devices.

Keywords: Conducting polymers: Nanofibers; Polymers.

Introduction:

In the recent years, nanofibers, nanorods, nanobelts, nanowires, and nanotubes like one dimensional (1D) nanostructures got tremendous research interest due to their exceptional applications in production of nanoscale devices as well as materials science. The quantum confinement and dimensionality of nanostructures are plays important role to investigate the electrical, thermal and mechanical properties. Nanofibers are hybrid nanocomposite materials formed by combination of organic and inorganic materials. These hybrid nanocomposite fibers are more homogeneous than other composites. Due to combination of organic and inorganic materials the nanofibers shows the properties of both materials like light weight, flexibility which belongs to organic materialsas well as high strength, thermal, andchemical stability which belongs to inorganic materials. Also, due to nano size these fibers represent some other properties like tremendous mechanical strength, different surface functionalities, tremendously large surface area, etc. (Banerjee and Kumar, 2011).

Nanofibers are prepared through the electrospinning (Electrospun) techniques.The high voltage source used in the electrospinning a technique which is connected to a needle

and metallic collector where the nanofibers are deposited. The needle act as positive electrode which connected to the polymer solution carrying injection pump and the metallic collector act as negative electrode. It makes the potential difference between needle and collector. The electrically charged jet (needle) used to throw out the composite solution as soon as the electric field surpasses the surface tension of drop. The solvent which used in solution is evaporated in throughout this procedure. The diameter of nanofiber range between 10-100 nm that could be achieve by changing rheological properties of composite solution and turning the processing parameters (Caratao *et al.,* 2014). The extra ordinary properties like high oxidizing power, low cost and non-toxicity attracts the tremendous research interest towards the Titanium dioxide (TiO2) doped composite materials. Also, it has application potential in gas sensors, solar cells, photocatalysis and biomedical applications (Hou *et al.,* 2015).

TiO_2 based nanofibers got tremendous research interest due to above mentioned properties and applications. TiO_2 based nanofibers represents the property of both organic and inorganic materials alone. TiO_2 based nanofibers are prepared by electrospinningsynthesis techniques. In this review article, the properties and applications of TiO_2 based nanofibers are discussed in detailed.

Characterization and Properties:

Ahmadpoor *et al.* (2013) investigated the morphologicaland optical properties of TiO_2 based polyvinyl alcohol (PVA) nanofibers. The scanning electron microscopy (SEM) and reflective spectrophotometer (RS) used to explore the optical properties. Less reflectance is observed through the reflectance spectra and increase in concentration of TiO_2 nanoparticle in composites decrease the reflectance as well as lightness. The interface surface reflectance affects the reflectance of pure PVA nanofibers. However, the internal scattering andinterface surface reflectance of TiO_2 nanoparticles affects the reflectance of TiO_2 doped PVA nanofibers. Madhavan *et al.* (2012) studied Electrical and optical properties of electrospun TiO_2-graphene composite nanofibers. These conductive nanofibers are prepared via electrospinning method and polyvinylpyrrolidone used as a carrier solution. The field emission scanning electron microscopy-energy dispersive X-ray (FESEM-EDX), transmission electron microscopy (TEM) was carried out for the morphological and structural investigation. X-ray diffractometry (XRD) was done to study phase analysis. The diameters and average surface pore sizes of the electrospun nanofibers were find out through the Raman spectroscopy, X-rayphotoelectron spectroscopy (XPS)

and Image analysis software. The mean specific conductance values obtained for TiO_2-graphene composites observed through the conductivity measurements represent the two times values than that of the electrospun TiO_2 nanofibers. Hou *et al.* (2015) synthesized the CuS decorated TiO_2 nanofibers through the mixture of electrospinning and hydrothermal processes as well as the polyvinylpyrrolidone (PVP)/tetrabutyl titanate Ti(OBu)4) was used as solvent. The photocatalytic activity was studied by degradation of methyl blue (MB) dye under illumination of light and the catalyst represents improved catalytic activity. The X-ray powder diffraction was done to find out phases and purity of the nanofibers. The surface morphology was investigated through the scanning electron microscopy and high-resolution transmission electron microscopy (HRTEM). UV-vis (Ultraviolet-Visible) spectrophotometer was used to investigate the UV-vis absorption spectra of TiO_2 fibers and CuS/TiO_2 fibers. The enhancement of light absorption in the UV and visible regions was observed through the optical properties of the CuS/TiO_2 heterostructure. CuS/TiO_2 nanofibers produce a higher charge separation. The suitable quantity of CuS doped in TiO_2 nanofibers contain improved photocatalytic activity observed via photodegradation measurement. This results represents the as-synthesized nanofibers have potential for photocatalytic and photovoltaic applications (Hou *et al.*, 2015).

Cartao *et al.* (2014) developed the Titanium oxide filled polyvinylpyrrolidone (PVP) composite nanofibers studied their thermal properties via thermal gravimetry analysis (TGA), differential thermal analysis (DTA). Surface morphology is investigated via SEM. Wu *et al.* (2009) prepared the Polyvinyl acetate/titanium dioxide($PVAc/TiO_2$) hybrid nanofibers through the two process electrospun and sol-gel method. The SEM, TEM and atomic force microscopy (AFM) technique is used to study the surface morphology as well as bulk structures oh hybrid nanofiber. These techniques confirmed the formation of $PVAc/TiO_2$ hybrid nanofibers. The chemical structure of$PVAc/TiO_2$ hybrid nanofibers are investigated with help of FTIR (Fourier transform infrared spectroscopy). Yang (2007) investigated cross-linked PVA/TiO_2 composite polymer membrane for alkaline direct methanol fuel cell (DMFC). Also, samples were characterized through TGA for thermal stability, SEM for surface morphology, ac impendence method for ac conductivity, XRD for structural confirmation as well as presence of TiO_2 in hybrid nanofibers. The cross-linked PVA/TiO_2 composite nanofibers can represents the great electrochemical performances at ambient temperatures and pressure. Also, as-synthesized nanofibers are used as electrode in Alkaline direct methanol fuel cell (DMFC). Kumar *et al.* (2007) investigated the structural

and optical properties of TiO_2-PVP (Titanium dioxide-poly(vinylpyrrolidone)) composite nanofibers synthesized via electrospun method. The surface morphology represents that the TiO_2 was uniformly dispersed in the PVP mixture the surface of nanofibers which was smooth and uniform. Moreover, along the fiber length the grains were tightly packed. Also, the cross section of the nanofibers was found to be circular solid and it investigated through the HRTEM technique. The selected area electron diffraction (SAED) pattern recorded at 200 kV, which represents the polycrystalline rings and was indexed for anatase TiO_2. The phase evolution of the TiO_2 in nanofibers examined via XRD patterns. Also, it reveals that as-synthesized nanofibers have amorphous nature. The review of literature represents the various characterization techniques used by different researchers and investigated the various properties of as-synthesized nanofibers. The study of surface morphology confirmed the size of prepared fibers.

Applications:

The TiO_2 based nanofibers represents various application potential which was reported by number of authors. The Titaniumoxide filled polyvinylpyrrolidone (PVP) composite nanofibers have application potential vast applicability such as catalytic devices, sensors, solar cells, cosmetics, scaffolds for tissue engineering, and optoelectronic devices (Caratao *et al.,* 2014). The cross-linked PVA/TiO_2 composite nanofibers represents extremely potential candidate for the DMFCapplications (Yang, 2007). The enormous potential for photocatalytic and photovoltaic applications were presents by the CuS based TiO_2 heterostructure (Hou *et al.,* 2015). The PVA/TiO_2 composite nanofiber has potential of application as an antibacterial and UV-protective nano-web (Caratao *et al.,* 2014). TiO2-graphene composite nanofibers can be utilizedas a photo-anode in dye sensitized solar cells (DSSCs)(Madhavan *et al.,* 2012; An *et al.,* 2014). These are the various potential applications reported by different researchers.

Conclusion:

The TiO_2 doped nanofibers are synthesized through the electrospinning technique and characterized via different characterization methods to examine its optical, thermal, electrical and other properties. The TiO_2 based composite nanofiber has potential of application various electronic devices reveals through the different investigation.

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CHAPTER
12

BASICS OF GENETIC ENGINEERING AND ITS APPLICATIONS IN RECENT ERA

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Genetic engineering:

It is the direct manipulation of an organism's genome (total no. of gene) using biotechnology. Novel DNA is inserted in the host genome by isolating and copying the gene of interest using molecular cloning method to construct a DNA sequence, or synthesizing the DNA and then inserting this new DNA in to the host organism.

One of the basic principles of recombinant DNA technology involves the digestion of a vehicle. For example, with plasmids or viral DNA restricting enzymes, which are molecular scissors that cut DNA at specific sites. DNA molecules from the juice organism are also digested in a separate tube with the same restriction enzyme. The two DNAs are then mixed together and joined together, this time using an enzyme called DNA ligase to form a single double-stranded DNA molecule. The vehicle containing the foreign DNA is then inserted into the recipient organism by transformation or transfusion. It is important to ensure that the vehicle has a replica origin, identified by the host's DNA synthesis machinery. After this the foreign DNA multiplies many times in the new host.

There are five essential elements to recombinant DNA technology:

1. Precise selection, cleavage and joining of DNA molecules obtained from different sources (donor DNA).
2. Attachment of recombinant DNA molecule to selected self-replicating gene vehicle (vector).
3. Transformation of a compound means recombinant DNA molecule into a host cell and selection.
4. Confirmation of cloned gene screening of the host by physical mapping and DNA sequencing.
5. Expression of a foreign gene in the host for the desired product.

Gene cloning Enzyme in r DNA technology:

1. DNA ligase:

- *E. coli* is the source of DNA ligase.
- Two fragments of DNA are joined by DNA ligase

2. Reverse transcriptase:

- mRNA template gives rise to complementary strand (cDNA) in the presence of RT.
- It is also known as RNA dependent DNA polymerase
- It is isolated from retrovirus

3. Restriction Enzyme: They are of two types:

(i) Restriction Exonucleases: They remove nucleotides from the ends of DNA.

(ii) Restriction endonucleases: They cut into specific locations within the DNA.

Thus, a restriction enzyme (or restriction endonuclease) identifies a specific base pair sequence in DNA called the restriction site and tears the DNA (hydrolyzes the posterior bone of the phosphodister) within the sequence. Restricted enzymes are widely found in prokaryotes and protect the host cell by destroying foreign DNA entering them. Here they function as part of a defense mechanism known as the Distraction Modification System.

Steward Lynn and Werner Arber (1963) isolated the two enzymes that cause the bacterium E. Inhibiting the growth of bacteriophages in E. coli.The discovery of this enzyme which have specific function in bacteria, uses restriction endonuclease to cut foreign DNA and protect themselves from viruses or other bacteria. Scientist W. Arber, H. Smith and D. Nathans were awarded Nobel-prize in1978 for discovery of this enzyme.

The restriction endonuclease enzyme identifies and cuts the DNA strand in a specific order called the restriction site. This enzyme is different from different types of microorganisms. When the microbial enters the cell the endonuclease enzyme degrades the foreign genome but the host cell's own DNA is protected from its endonuclease by the base methylation at the restriction site.

There are 5 types of restriction endonucleases as: Type I, Type II, Type III, Type IV and Type V.

Type I Restriction Endonuclease: (Restriction and Modification)

- It has both methylation and endonuclease activity.
- It require ATP to cut the DNA
- It slices DNA at about one thousand bp away from its restriction site
- eg.EcoKI

Type II Restriction Endonuclease:

- ATP is not needed to cut DNA
- It cuts DNA at restriction site itself (short4-9bps)
- eg.EcoRI, Hind III

Type III Restriction Endonuclease:

- It requires ATP to cut DNA
- A cut is made 25 bp away from restriction site. eg.EcoPI

Type IV Restriction Endonuclease:

- Recognize modified, typically modified, typically methylated DNA Exemplified by McrBc and Mrr system of *E. coli*

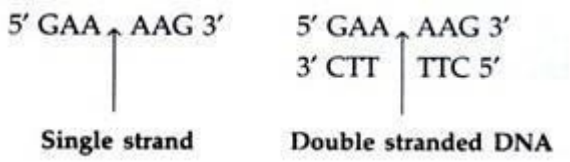
Type V Restriction endonuclease:

- It can cut DNA of various lengths provided that a suitable guide RNA is provided.
- E.g. The cas9-gRNA complex.

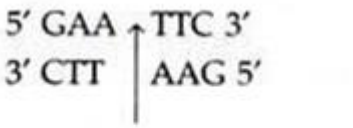
Table 1: Some examples of type II restriction enzymes along with sources and recognition sites on sequences

S. No.	Restriction enzyme	Source	Sequence with recognition sites
1.	*Eco* RV	*Escherichia coli*	5′ GAT↓ATC 3′ 3′ CTA↑ TAG 5′
2.	*Alu*I	*Arthrobacter luteus*	5′-A-G↓C-T-3′ 3′-T-C↑G-A-5′
3.	*Bam*HI	*Bacillus amyloliquefaciens*	5′G↓G-A-T-C-C-3′ 3′C-C-T-A-G↑G-5′
4.	*Eco*RI	*Escherichia coli*	5′G↓A-A-T-T-C-3′ 3′C-T-T-A-A↑G-5′
5.	*Eco*RII	*Escherichia coli*	5′↓C-C-T-G-G-3′ 3′-G-G-A-C↑C-5′
6.	*Pst*I	*Providencia stuartii*	5′-C-T-G-C-A↓G-3′ 3′-G↑A-C-G-T-C-5′
7.	*Sal*I	*Streptomyces albus*	5′-↓G-T-C-G-A-C-3′ 3′-C-A-G-C-T↑G-5′
8.	*Bam* HI	*Bacillus amyloliquefaciens*	5′-GACNN↓NGTC 3′ 3′ CTG NNNCA↑G 5′

Recognition sequence for type II restriction enzymes creates palindromes with rotational symmetry. In the palindrome, the base sequence of the second half in the DNA strand represents the mirror image of the base sequence of the first half. Because of this in the DNA double helix, the complementary strand also represents the image of the same mirror.



Palindromes are groups of letters that form similar words when read both front and back, such as 'Malayalam'. In contrast to the palindrome, when the same word is read in both directions, the palindrome in DNA is a sequence of base pairs that read the same on two strands while the direction of reading is kept the same.



Eco RI recognition site
An example of pallindrome with rotational symmetry.

Eco RI cuts the DNA molecules of two plasmids due to identical spots in their DNA. The spherical form of DNA becomes linear in both cases. Such linear DNA can stick together to form a single recombinant DNA molecule.

4. Terminal transferase:

- It is the enzyme that converts the dull ends of DNA fragments into sticky ends.
- Efficiency if the restriction enzyme cuts off the end of the DNA-forming apoptosis, the bond is very low. The enzyme terminal transfer therefore converts the bunt end to a sticky end.
- The terminal transfer enzyme synthesizes a short sequence of complementary nucleotides on the free end of DNA, so that the blunt end is converted to the sticky end.

5. Nuclease:

- The enzyme nuclease hydrolyzes the phosphodiesterbonds on the DNA strand forming the 3’-OH group and 5’-P group.

- It usually cuts the DNA on both sides of the deformation caused by thymine dimers or intercalating agents.
- Gap is filled by DNA polymerase and strands are joined by DNA ligases
- There are two types of nuclease; Endonuclease and exonuclease

6. DNA polymerase:

- DNA polymerase is a complex enzyme that synthesizes complementary nucleotides of the template strand.
- It adds nucleotides to the free 3 ′ OH end and helps to lengthen the strand
- It also helps to fill gaps in double stranded DNA.
- DNA polymerase-I isolated from E. coli commonly used in gene cloning.
- Taq polymerase from Thermus aquatics is used in PCR

7. Ribonuclease-H (RNase H):

- DNA-RNA heteroduplex gives away mRNA in the presence of RNase-H which is used to synthesize cDNA.
- It is isolated from retrovirus

8. Alkaline phosphatase:

- The enzyme alkaline phosphatase helps in removal of terminal phosphate group from 5′ end
- Self annealing of vector DNAis prevented.

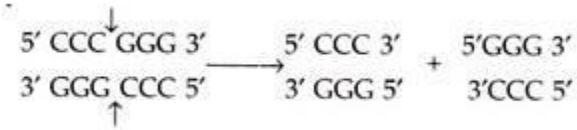
9. Polynucleotide kinase:

- It adds phosphate group from ATP molecule to terminal 5'end after dephosphorylation by alkaline phosphatase

Types of Cleavage Produced By Restriction Enzymes:

Many restricted enzymes such as seratiamarscens cleave both strands of small isolated DNA from the identical nucleotide location in the center of the recognizable space resulting in a blunt or flush end.

The small 6 nucleotide recognizes the palindromic sequence and cleaves at both ends.



Splicing and cloning of genes:

Due to Biotechnological tools scientist can identify specific gene sequence, remove them and made clone and use in different organism to obtained desired products. This whole process involves gene Splicing and Cloning which includes following steps.

1. Specific Selection, Isolation by Cleavage: Gene of interest is identified, selected and isolated by restriction digestion which cleave gene from donor genome and then purified.
2. Selection of Vector and restriction digestion i.e. splicing: Suitable vector is selected and cut by same restriction endonuclease enzyme called splicing.
3. Ligation of rDNA molecule to a Vector: Insertion of gene of interest in to vector done by ligation by DNA ligase which attaches two different DNA molecules. Thus the target gene of interest is incorporated in to suitable vector. The hybrid DNA is now called as rDNA molecule.
4. Cloning: Many copies of desired gene can be obtained by placing them in to a host cell with the help of vector. The desired gene with the vector replicates and generating more number of copies of recombinant molecules called Cloning.
5. Gene transfer: The gene of interest is now transferred to host cell and transferred cell is selected, multiplied and are introduced to produce transgenic plants and animals.
6. Expression of desired Gene: The gene of interest expresses in another genome of host thus desired trait i.e. characters are expressed result in to desired product.

Due to cloning amplification of rDNA can be possible in the host which is genetically identical copies in the organisms, this all of which contains the r DNA molecules that can be propagated and grown in bulk hence amplifying the rDNA molecules and any gene product whose synthesis is direct.

Cloning Vehicles (Vector):

A vector is a DNA molecule that has the ability to replicate in a host cell and is integrated into a DNA fragment called a DNA insert to clone. Cloning of a foreign fragment of DNA into bacteria is made possible by the ability of vectors or "carriers" to continue their way of life after inserting additional sequences of DNA into their genomes. The insertion results in a "hybrid" or "chimeric" or "recombinant" vector that contains part of the extra "foreign" part of the DNA.

This chimeric vector, when cloned into bacteria, mimics the original vector in exactly the same way and is therefore obtained in large quantities. In this way, the inserted

foreign DNA simultaneously replicates with the rest of the chimeric vector and copies of the original foreign DNA can then be obtained from the offspring.

Three basic attributes are there in Cloning plasmid vector:

(i) Low molecular weight, small in size.

(ii) The ability to easily provide selective phenotypic traits on host cells, and

(iii) Some sites for large number of restriction enzymes.Relaxed replication control.

The benefits of low molecular weight are many. The first plasmid is very easy to handle. Second, low molecular weight plasmids are usually present as multiple replicas. Finally, plasmids with low molecular weight are less likely to contain restriction enzymes.

Practical applications of biotechnology and genetic engineering in animals:

There are many things that can be done more effectively with the help of cloning techniques. These include gene mapping, controlled mutagenesis, and production of specific gene products. However, with the development of DNA cloning came a major revolution in eukaryotic biology that allows for the separation and characterization of defined parts of any DNA. Some of the applications of this technology in medical, veterinary, agricultural science and industrial applications have been discussed which could facilitate or greatly facilitate through DNA cloning.

Medical and veterinary applications:

Diagnosis of genetic disease: One of the main medical applications of gene cloning is to safely predict or diagnose genetic diseases in the fetus, which is incurable through the available therapeutic strategies to offer abortion to prevent the birth of incurable sick children. Some of the genetic diseases that can currently be diagnosed before delivery are various enzymopathy including a congenital metabolic defect. E.g., Te Sacks Disease, Gauchers Disease, Hurlers Syndrome, Galactosemia, Hypercholesterolemia, Lash-Nyahan Syndrome, XerodemaPigmentosis, Figmentosis, Figmentosis. Hemoglobin diseases such as sickle cell anemia and thalassemia.

Gene therapy:

It corrects a congenital defect in metabolism by inserting normal genes of somatic or germ cells into the affected organism. In somatic therapy, healthy copies of genes are inserted into somatic cells that are not involved in reproduction, and such mutations are not passed on to future generations. In contrast, germ-line therapy treats cells that produce eggs and sperm, thus affecting all future offspring. In gene therapy, cells need to be removed from the body, cultured, genetically manipulated, and then replanted in the

patient from whom the original tissue was taken. The first human experiment was conducted at NIH in 1990.

Agricultural Applications:

Recombinant DNA technology is being used to increase plant yields, resist disease or pollution, and create new crops that can utilize previously wasted resources. The new gene can be inserted into the bacterial DNA section to transfer to plant cells.

Improving yields:

There are various ways to increase yields. You can aim for either a faster growth rate, a more efficient use of nutrients, or an increase in the amount of food produced by plants in case of cereal crops like wheat or rice.

Novel Crops:

One of the problems of modern agriculture is that crops are often grown hundreds or thousands of miles away from the consumer. In the case of tomatoes, the problem may now be solved, with researchers now producing tomatoes that are softer and more resistant to rot after ripening.

Production of Drugs:

Perhaps the most compelling aspect of recombinant DNA technology is its use for the production of microorganisms that synthesize human proteins with therapeutic potential as this technology can produce more antibiotics, reducing production costs. Other examples are human insulin, the human growth hormone (somatostatin) and the antiviral agent, interferon, which is being marketed. Many more are under clinical trial.

Production of synthetic vaccines:

The development of synthetic vaccines is a major breakthrough in disease prevention. Attempts have also been made to use genetic engineering to facilitate vaccine production. Some vaccines, such as anti-hepatitis B, are difficult to produce because of the high risk of dealing with the virus in large quantities.

Food industries:

We have already seen how recombinant DNA technology affects food production under standard agricultural conditions. We now turn to other sectors of the food industry that are using this technology.

Forensic science:

When investigating a criminal offense, such as burglary, serious sexual assault or murder, police try to find evidence that shows who the perpetrators are. Recombinant DNA technology is now used in a variety of ways.

Probable hazards in animals:

Benefits are counted much as compare to hazards from Biotechnology. Point to be discussed about environmental, health, legal, ethical, social, and technological risk of this technology.

1 Health:

Human and animal health may affected by consumption of Biotechnological products. Some allergies, toxicity, nutrient imbalance, decrease of food diversity are seen biotechnological products.

2. Ethical issues:

1. We do not understand the nature of genes and their origin, evolution and their role in the shape of various organisms.
2. We do not fully understand the size and role of genetic exchange between different species.

Content We should not experiment with transgenic organisms

3. As a result of a large number of genes and environmental factors, we do not take into account the phenotype properties of the largest number of humans by which people differ.
4. Information related to genetics should be used exclusively to allow everyone to make individual decisions about lifestyle.
5. The creation of biological weapons outside the phenomenon of bioterrorism.

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CHAPTER
13

CONTRIBUTION OF COMPUTATIONAL BIOLOGY IN COVID-19 RESEARCH

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Introduction:

After the sequencing of insulin peptides in the 1950s [1, 2, 3], computational biology emerges as a crucial interdisciplinary field in biological sciences. Today's scientific realm focused on the generation of larger biological databases and their implications for a wide array of disciplines like comparative genomics, functional genomics, molecular epidemiology, drug designing, molecular diagnostic, etc. Computational Biology provides opportunities to analyze a larger amount of biological data with more precision and accuracy. Recent advances in computer programming and molecular biology have potentially contributed to the emergence of computational biology, powered by stringent mathematical and statistical modelling. In the current pandemic, computational biology proves its magnitude in a wide array of applications. Virology labs throughout the world strictly focused on the production of molecular databases, widely utilized in a range of studies right from variant identification to vaccine and drug designing. Computational Biology along with Artificial Intelligence (AI) powered the molecular epidemiology in all the dimensions. The prime aim of this chapter is to cast light on a) Vaccine Design b) Drug Discovery c) Prediction of Disease, with reference to Computational Biology.

The coronavirus disease 2019 (COVID-19) is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which is the outcome of zoonotic origin in Wuhan, China, which later converted to a global pandemic. The novel coronavirus also called SARS-CoV-2, has a single-stranded, positive-sensed RNA genome with approximately 29.9-kilo base pairs, encoding the spike (S), envelope (E), membrane (M), and nucleocapsid (N) structural proteins with other non-structural proteins [4–6]. The life cycle of the virus started by binding its S protein to ACE2 (Angiotensin Converting Enzyme 2) receptors, following the transfer of the viral genome into the cytoplasm. Considerable research has been carried out for vaccine development and drug designing [7, 8]. But complete immunization and the evaluation of therapeutic efficacy still remain neglected issues that can be tackled by computational and structural biology. Development in

artificial intelligence (AI) with machine learning and Data sciences powered computational biology, which is further revolutionizing the areas of biology, medicine, and public health. The computational biology tools are widely utilized for drug designing and screening, vaccine design, and the real-time dynamics COVID-19 pandemic. Availability of genomic data utilized as a piece of raw information for vaccine and drug designing.

1. Vaccine Designing:

Vaccines are one of the most effective discoveries in modern medicine, after the first use of a vaccine against smallpox in 1796 by Edward Jenner's. According to recent data, more than 70 vaccines have been developed and licensed which are effectively used against approximately 30 microbes. Vaccines are considered as the least expensive and most simplistic way of protection against shattering epidemics, providing the most cost-effective way to save lives in epidemics. Vaccines are the attenuated fragments of the antigen, containing other ingredients that keep the vaccine safe and effective. The prime function of vaccine component serves a specific purpose of producing the immunity, and each ingredient is tested in the manufacturing process. In recent days, the Reverse vaccinology is improved vaccinology which is based on bioinformatics and reverse pharmacology practices. The pioneer of reverse vaccinology is Rino Rappuoli and this approach was used against Serogroup B meningococcus for the first time.

Artificial Intelligence and machine learning algorithms have been widely utilised in reverse vaccinology. Software such as NEC Immune Profiler [9], the newly developed neural network-based ArdImmune Rank model [10], and the eXtreme Gradient Boosting (XGBoost)-based Vaxign-ML model [11,12] have been used to identify immunogenic epitopes from the SARS-CoV-2 proteome. These approaches may provide significant help in designing multiepitope chimeric vaccines with theoretically higher. There are four major categories of COVID Nucleic Acid (RNA AND DNA), Whole Virus, and Protein Subunit.

a) Messenger RNA (mRNA) vaccine: In this type, the nucleic acid is use as a precursor molecule for immunization. This vaccine is made up of genetically engineered mRNA which instructs cells to make the S protein of the COVID-19 virus. After vaccination, the starts the synthesis of S protein and displaying those on cell surfaces that results in the production of specific antibodies. By this way, the body launch its immune response, if it later became infected with the COVID-19 virus. After delivering instructions, the mRNA is immediately cleaved down and never enters the nucleus of the cells. Both the

Pfizer-BioNTech and the Moderna COVID-19 vaccines use mRNA, which are some of the first COVID-19 vaccines authorized and approved for use in the United States.

b) Vector vaccine: In this type of the vaccine, the genetic material obtained from the COVID-19 virus is modified as a viral vector and when these viral vectors gets inside the body, it transfers the genetic material of COVID-19 virus, which will be the source of instructions to make copies of the S protein. When S proteins forms and displayed on the cell surfaces, immune system starts responding by creating antibodies and defensive white blood cells. If you later become infected with the same virus, the antibodies will again fight the virus. The Janssen/Johnson & Johnson COVID-19 vaccine and AstraZeneca in collaboration with University of Oxford produced the vector COVID-19 vaccine.

c) Protein subunit vaccine: In this type of vaccine the parts of the virus are used to stimulate the host immune system containing, attenuated S proteins, which will instruct the cells for immunization. Once the immune system recognizes the S proteins, it creates antibodies and defensive white blood cells. Novavax is the protein subunit COVID-19 vaccine and U.S. COVAXIN.

The indigenous COVID-19 vaccine developed by Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). This vaccine is developed and manufactured by Bharat Biotech. This vaccine is developed by Whole-Virion Inactivated Vero Cell derived platform technology containing attenuated dead virus, unable to infect people but able to instruct the immune system to launch a defensive immune system against virus. This vaccine does not replicate and do not revert and cause pathological effects. In India, the Oxford–AstraZeneca vaccine manufactured by Serum Institute of India under the trade name Covishield also developed and distributed. The Serum Institute of India and Indian Council of Medical Research are jointly conducted the Phase II/III, Observer-Blind, Randomized, Controlled Study to Determine the Safety and Immunogenicity of Covishield (COVID-19 Vaccine), after which this vaccine is distributed throughout India for vaccination with COVAXIN. Till date, total, 188Cr doses are provided in India, out of which 85.1Cr Indian citizens are fully vaccinated.

2. Drug Discovery:

During this pandemic, finding a novel active antiviral drug was the biggest challenge. In recent days, computational modeling using molecular docking screening and molecular dynamics simulations have been extensively used approach to discover compounds that target SARS-CoV-2 proteins. In some published studies, the compounds

including terpenes NPACT01552, NPACT01557, and NPACT00631 [13], Mpro inhibitors tinosponone [14], ChEMBL275592, montelukast, ChEMBL288347 [15], quercetin-3-O-rhamnoside [16], and biflavone amentoflavone [17], RNA-dependent RNA polymerase (RdRp) inhibitors Galidesivir and the two drug-like compounds CID123624208 and CID11687749 [18] are identified that binds SARS-CoV-2 receptor-binding domain (RBD). The study reveals that plant secondary metabolites like flavonoid glycosides, biflavonoids, ellagitannins, anthocyanidins, and triterpenes could be used as a TMPRSS2, SARS-CoV-2 S, Mpro and RdRp inhibitors [19]. While the study uses molecular docking with machine learning to further expedite the screening procedure and identified six potential Mpro inhibitors from over 2000 natural compounds [20]. The widely used computational methods based on network-based or expression-based algorithms and docking simulations have also been widely applied during the pandemic to identify candidates for drug repurposing [21, 22]. The incorporation of computational methods including AI platforms could make it possible to screen more efficient large-scale data, and in vitro validation further improve the accuracy of platforms. A deep neural (DNN) constructed by [23] Ke et al. to screen previously identified antiviral drugs against SARS-CoV, Influenza virus, and human immunodeficiency virus (HIV) or known 3CLpro inhibitors. These predicted drugs are validated in vitro with a similar feline coronavirus, feline infectious peritonitis (FIP) virus, and reconfigured by an AI algorithm for future predictions [23]. AI can be used to countercheck the efficacy of different combinations of approved drugs and their effects. These are the review of a few studies, there are a lot of different approaches and studies going on to discover COVID-19 drugs, in the future the findings of these studies will potentially contribute to counterchecking the current pandemic.

3. Prediction of epicentres and outbreaks:

Machine learning approaches are also used to investigate, predict and countercheck the ongoing COVID-19 pandemic. A variety of algorithms including long short-term memory (LSTM) network [24–27], Grey Wolf Optimizer (GWO)-LSTM hybrid model [28], autoregressive integrated moving average (ARIMA) [29-31], XGboost [32], support vector regression (SVR) [33,34], and genetic programming [35] were used to understand the confirmed cases, recovered cases, and death in affected countries. These models are applicable in predicting COVID-19 transmission and could contribute to producing baseline statistical data that will use in policy-making to prevent new outbreaks.

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CHAPTER
14

TARGETED GENE THERAPY – A REVOLUTION IN HEALTHCARE

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'Gene therapy' can be described as the mode of treatment where modifications of the genome that repair or restore the normal functioning ofimportant gene or to suppress the function of a gene causing a disease. Nowadays this therapy is growing rapidly due to practical perspective and applicability to treatment of major human diseases. Recently, targeted strategies for gene therapy are developed that corrects a cell's own repair pathways to repair or disrupt a target gene.

Recombinant DNA (rDNA) technology, (1) firstly paved roots for the gene therapy and progressed with the development of genetic engineering tools, such as viral vectors. (2-4). Since the early 1990s the huge number of clinical trials (about 1900) have been conducted having gene therapeutic approaches. These include insertion of DNA randomly into the host genome using conventional genetic engineering tools.

In the coming days, many tools were developed which will be discussed further in the chapter. Before exploring recent scenario, lets dwell a little into history and basics of this field.

Gene - basic unit of heredity:

Basic unit of heredity is gene.Long strands of a molecule called DNA makes up Genes which are situated in the chromosomes. Nucleotides are formed from Specific linear arrangement of DNA, which eventually forms genetic message. The ordered sequence of nucleotides located in a particular position on a particular chromosomeencodes a specific functional product. The product may be a protein or an RNA molecule.

Genes are transferred from the parents to the next generation, they bring about inheritance and determines the unique traits - like the colour of the eyes and colour and texture of the hair (5). A unique sequence of nucleotides forms genetic makeup of each individual, thismakes every human being unique.

An imperfection or error (referred as mutation) in any one of these genes can result in anabnormal condition, disease, physical disability or shortened life span. These genes as described earlier can be passed from one generation to other causing mutations to get

inherited just like a mother's eye colour or fathers' height. But with advent and evolution of gene therapy, the treatment or elimination of inherited diseases or physical conditions due to these imperfect genes could become a reality (6).

Modes of gene therapy:

- Anengineered normal gene may be incorporated into a location within the genome to replace aincorrect gene.
- Homologous recombination can be done to change mutated gene for a normal gene.
- Return of the gene to its normal function can be done by repairing abnormal gene through reverse mutation.
- Particular gene is regulated to the degree it should expressonly as per need inside the cell.

History of gene therapy:

In early days raw formed techniques were into existence and with the evolution of science, sophisticated and precise procedures came into existence which eventually benefitted immensely to healthcare. The brief history and important events in the advancement of gene therapy can be shown in the table below (Table credits Tamura *et al.,* 2020) (7)

Table 1 History of gene therapy

Year	History of GT
1962	Successful transformation of human cells with genomic DNA was achieved.
1970	Treatment strategy using viral vectors was developed.
1972	The concept of GT was established. Technologies using recombinant DNA were developed.
1974	Advisory committee was established for recombinant DNA
1980	Unapproved GT was performed.
1981	Retroviral vector was developed.
1983	Non-replicating retroviral vector was developed.
1986	Guideline of GT was established.
1989	A marker gene was first transduced into patient TILs using a retroviral vector.

History of GT for hereditary disease		History of GT for malignant tumor	
1990	GT was performed for patients with ADA deficiency.	**1992**	GT was first applied for malignant tumors (glioblastoma).
1999	A patient with OTC deficiency died after receiving GT.	**2006**	TCR therapy was effective for the patients with melanoma.
2002	Leukemia was observed in patients with X-SCID after GT.	**2013**	CAR-T showed excellent clinical efficacy for hematological malignancies.
2008-2011	The effectiveness of GT was reported for patients with LCA, ALD, and Hemophilia B.	**2015**	Imlygic was approved for melanoma GT.
2012	A GT-based drug (Glybera) was first approved for LPL deficiency.	**2017**	Two CD19-targeting CAR-T cell products, Kymriah and Yescarta, were approved for B-ALL and DLBCL, respectively. Luxturna was approved for the patients with LCA.
2016	Strimvelis was approved for treatment ADA deficiency.		
2019	Zolgensma was approved for SMA.		

ADA: adenosine deaminase, ALD: adrenoleukodystrophy, B-ALL: B cell acute lymphoblastic leukemia, CAR: chimeric antigen receptor-modified, DLBCL: diffuse large B-cell lymphoma, GT: gene therapy, LCA: Leber's congenital amaurosis, LPL: lipoprotein lipase deficiency, OTC: ornithine transcarbamylase, SCID: severe combined immunodeficiency, SMA: spinal muscular atrophy, TCR: T cell receptor, TIL: tumor infiltrating lymphocyte.

Gene therapy types:

1) First type is Somatic Gene therapy where a 'Good' gene is inserted in the somatic cells thus this will only help the patient and not its offspring. Thus the progeny of patient still have chances of expressing the disease.

2) Germline gene therapy entail injecting foreign genes into fertilized eggs or in sperms producing cells, which will then pass any genetic changes to future generations as well. This therapy is not practiced widely because many technical and ethical issues (8).

Various methods of gene therapy:

Many methods are practicedin gene therapy, most of which are listed below

1) Physical
    a) Direct injection of DNA
    b)LiposomemediatedDNAtransfer
    c) Calcium phosphate transfection
    d) Electroporation
2) Retrovirus vectors
3) Other viral vectors
4) Targeted gene transfer via receptors
5) Artificial chromosomes
6) Site-directed recombination
7) Activation of genes of related function

Beginning of gene therapy using viral vector:

Through onset years only nonviral methods, such as microinjection and calcium-phosphate precipitation, were used for gene delivery. Nonviral methods yielded lower levels of transfection and gene expression, resulting in limited therapeutic efficacy (9).Viruses encapsule and deliver their genes to human cells in a pathogenic manner. With the passage of time viral vectors emerged to be crucial components in the manufacture of cell and gene therapy. Currently, the most common used vector is a virus that has been genetically modified to carry normal human DNA.(10) few of the different types of viral vectors used in gene therapy (11,12).

- Retroviruses - A class of viruses that can create double-stranded DNA copies of their RNA genomes by a process called reverse transcription, Human immunodeficiency virus (HIV) is a retrovirus. These double stranded copies can be integrated into host Chromosomes.
- Adenoviruses - A class of viruses with double-stranded DNA genomes for example common cold virus is an adenovirus.

- Adeno-associated viruses –These viruses insert their genetic material at specific site on chromosome 19, these are small, single-stranded DNA viruses.
- Herpes simplex viruses - Particular cell type is infected by these viruses likeneurons (8).

Genome editing - A new technology:

Genetic engineering technologies using viral vectors to randomly insert therapeutic genes into a host genome. This raised concerns about insertional mutagenesis and oncogene activation. Thus, new precise technology to intentionally insert genes at site-specific locations was needed. Moving forward a more advance, precise and reliable technique is evolved and is currently practiced in majority of labs. In this technique Bioinformatics plays a significant role.

Genome editing tools:

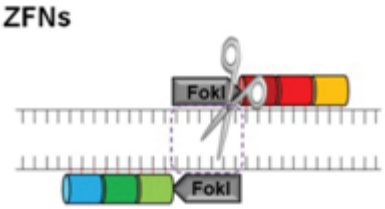
There are main 3 tools which came in existence recently.

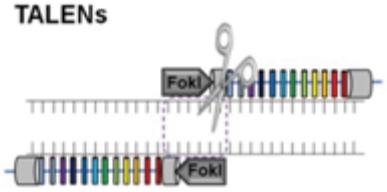
1. ZFNs are fusions of the nonspecific DNA cleavage domain of the Fok I restriction endonuclease and zincfinger proteins that lead to DNA double-strand breaks (DSBs).A trinucleotide DNA sequenceis recognised by Zinc-finger domain (Fig. 1). However, design and selection of zinc-finger arrays is difficult and time-consuming (13).
2. TALENs are fusions of the Fok I cleavage domain and DNA-binding domains derived from TALE proteins. TALENs have ability to recognize a single base pair, leading to precise accuracy (Fig. 2) (14).

The CRISPR/Cas9 system consists of Cas9 nuclease and two RNAs (CRISPR RNA [crRNA] and transactivating CRISPR RNA [tracrRNA] (15) The crRNA/ tracrRNA complex (gRNA) induces the Cas9 nuclease and cleaves DNA upstream of a protospacer-adjacent motif (PAM, 5'-NGG-3' for S. pyogenes) (Fig. 3). Currently, Cas9 from S. pyogenes (SpCas9) is the most popular tool for genome editing (16). (Table credits R. Tamura et al-7).

Table 2 Characteristics of genome editing technologies

	ZFNs	TALENs	CRISPR/Cas9
Length of recognized DNA target	9–18bp	30–40bp	22bp + PAM sequence
DNA recognition	Multimeric protein-DNA interaction	Protein-DNA interaction	RNA-DNA interaction
Nuclease design	Difficult	Feasible	Easy
Cost	High	Moderate	Low
Success rate of nuclease design	Low	High	High
Potential off-target effects	Yes	Yes	Yes
Specificity	Moderate	High	Moderate
Sensitivity to DNA methylation	Not known	Sensitive to CpG methylation	Not sensitive to CpG methylation





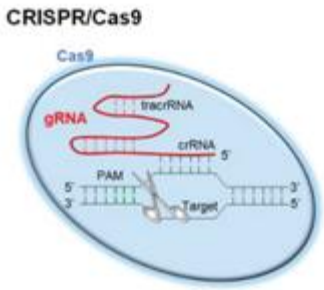


Figure 1 **Figure 2** **Figure 3**

Figure - Genome editing tools. Three types of genomes editing tools including ZFNs, TALENs, and CRISPR/Cas9 are shown. (Figures adapted from R. Tamura et al-7)

Fig 1 - ZFNs are hybrid proteins using zinc-finger arrays and the catalytic domain of FokI endonuclease.

Fig 2 - TALENs are hybrid proteins containing the TAL effector backbone and the catalytic domain of FokI endonuclease.

Fig 3 - The CRISPR/Cas9 system is composed of Cas9 endonuclease and sgRNA. Cas9: CRISPR-associated-9, CRISPR: clustered regularly interspaced palindromic repeats, sgRNA: single-guide RNA, TALENs: transcription activator-like effector nucleases, ZFNs: zinc-finger nucleases.

Criteria for selection of Disease

Eve Nichols describes the criteria for selection of disease for human gene therapy (17):

1) The disease is an incurable, life-threatening disease;
2) Organ, tissue and cell types affected by the disease have been identified
3) The normal counterpart of the defective gene has been isolated and cloned
4) The normal gene can be introduced into a substantial sub fraction of the cells from the affected tissue; or that introduction of the gene into the available target tissue, such as bone marrow, will somehow alter the disease process in the tissue affected by the disease.
5) The gene can be expressed adequately (it will direct the production of enough normal protein to make a difference)
6) Techniques are available to verify the safety of the procedure.

Examples of successful clinical trials of gene therapies:

Below are some gene therapy success stories.Researchers have been working for decades to bring gene therapy to the clinic, still very few patients have received any effective gene-therapy treatments. Even though gene therapy has been slow to reach patients, its future is very promising.Today, many clinical trials are underway, where researchers are carefully testing treatments to ensure that any gene therapy brought into the clinic is both safe and effective. (18)

1. Immune deficiencies

Many immune deficiencies that inherit form one generation to other have been treated successfully with gene therapy.One more condition recognised by deficiency of adenosine deaminase has been successfully treated with this therapy.

2. Hereditary blindness

Many degrative forms of inherited blindness have been treated with this therapy. Results show that therapy has potential to slow or even reverse vision loss.

3. Hemophilia

Haemophilia disease makes blood clots impossible causing fatal situations with even minor cuts and bruises to the patient. Some major proteins that help their blood form clots are missing in them. This form of life-threatening disease has been successfully treated with this therapy.

4. Blood disease

Beta-globin gene which codes for oxygen-carrying protein in red blood cells is defective in the patients. Thus, patients don't have enough RBC's which makes patients severely ill. Patientswith sickle cell disease can also be treated with similar method.

6. Cancer

Many approaches have shown promise in treatment of cancer. Thus, lifespan of patients has been increased substantially by the virtue of this therapy.

7. Spinal muscular atrophy (SMA) (19)

It is a rare, progressive neuromuscular disease caused due to mutationsin survival motor neuron 1 (SMN1) gene. This causes muscle weakness and loss of muscle mass, and in severe cases, respiratory failure and death (20).

Advance research in the field has produced following drugs which have shown great success in patients who were treated in the early stages of life. In 2016 Nusinersen was the first therapy approved by the FDA. Further in 2019 Zolgensma® has been approved by

FDA as the second disease modifying SMA treatment for patients aged up to 2 years old with SMA type I (21).Recently, risdiplam (Trade name: EvrysdiTM) was approved by the FDA as the first oral drug for SMA patients (22).

Limitations of targeted drug therapy:

- There are few the limitations to the treatment such as viability, long-term effects, side effects. Cost, among others, are highlighted. Moreover, elevated costs of drugsplace this drug among the most expensive drugs.
- Cost of single dose of SMA drug costs around 16 Crore Indian Rupees.
- Most of the favourable characters of viral vectors also put threat with their pathogenic activities.
- Viruses may cause toxicity, immune and inflammatory responses, and gene control and targeting issues.
- One constant fear is that viral vector once inside the patient may regain its original disease-causing capacity.
- Multigene disorders - Such as heart disease, high blood pressure, Alzheimer's disease, arthritis, and diabetes, are caused by the synchronous action of many genes, however currently gene therapy works better for single gene disorders.
- We may conclude that gene therapy is still in its primitive stages but in future it may replace many famous widely used aspects of other therapies and this therapy thus shows promising future.

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CHAPTER
15

AN OVERVIEW OF EXPERIMENTAL STUDIES ON METALLIC NANOREFRIGERANTS

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Abstract:

This review paper is primary attempt to study recent developments in metal oxide nanoparticle based nanorefrigerants. Nanorefrigerants as a heat transfer fluid becomes very popular due to their versatile thermo-physical properties such as pressure reduction in nanorefrigerants, boiling heat transfer and exposure to nanorefrigerants in various local refrigerators. Therefore, nanorefrigerants become the burning topic of research for researchers across the globe. Many research reports show that adding nanoparticles improves system performance and energy efficiency.

Keywords: Nanofluid; Nanorefrigerants; Metal oxide

Introduction:

The shortage of energy and global warming are the major problems present days that may disturb the sustainable development of human society.In a steam compression refrigeration system, the compressor is the primary source of energy consumption. Reducing the work of compression is an effective way to solve the problem of energy shortage. In terms of environmental protection, high global warming impact refrigerants (CFCs and HFCs etc.) is being replaced by very low or zero global warming impact refrigerants such as R290 and R600a. The use of nanoparticles in refrigeration and air conditioning systems is another way to solve the problem of energy consumption by compressors. The use of nanoparticles in the refrigerant or in the lubricating oil of the compressor may increase the solubility between the refrigerant and the lubricating oil mixture in the cycle.

However, there are some penalties for using nanoparticles in the refrigeration system, such as pressure drop and increase in pumping power. Peng *et al.* [1] established a correlation to predict the frictional pressure drop of nanorefrigerant. They showed that viscosity of nanorefrigerant is directly related to pressure drop and pumping power. The thermophysical properties and flow properties are important to estimate the effectiveness

of a nanofluid or a nanorefrigerant [2]. The thermal conductivity, viscosity, specific heat, latent heat, density and surface tension are some of the most important thermophysical properties of a fluid. Much of the research in the past has focused on the thermal conductivity of nanofluids. But recently, studies based on viscosity have also come out. It is important to extend this research to other thermophysical properties since it will give a better idea of the heat transfer performance of nanorefrigerants [3]. Heat transfer performance is directly related to the thermal conductivityof a substance. Therefore, selection of materials play important role. In this betterment of refrigeration systems, nanomaterials plays very key role. Literature survey shows that nanomaterials like Al_2O_3, TiO_2, CuO, ZnO, Graphene and Carbon nanotubes (CNT) have ability to improve heat transfer performance of base refrigerants such as R134a, R600a, R141b etc.

Aggregation and sedimentationof nanoparticles in the refrigerant-based nanofluid may reduce thestability of refrigerant-based nanofluid and limit the application ofrefrigerant-based nanofluid in the refrigeration system. Since then, numerous studies have been conducted on the thermophysical and heat transfer performance of nanorefrigerants. Literatures show that thermalconductivity and heat transfer performance can be increased bysuspending nanoparticles in refrigerants [4, 5].

Noteworthy reports in literature:

Wang *et al.* [6] did an experimentalstudy on pool boiling heat transfer characteristics of Al_2O_3nanoparticles dispersed in R22 refrigerant and observedthat nanoparticles enhanced the heat transfer characteristicsof the refrigerant R22.In an experimental study, Bobbo *et al.* [7]studied the effect of dispersion of titanium dioxidenanoparticles and single wall carbon nanohorns on the tribological properties of commercial Polyester oil.The results showed that TiO_2/POE mixture has best performanceas compared with the pure polyolester oil and carbon nanohorns /polyolester oil.Bi *et al.* [8] experimentally investigated the performance ofTiO_2 nanoparticles in domestic refrigerator. The resultsshowed that 0.1 % of TiO_2 nanoparticles in R134a and POEoil system reduced the power consumption by 26 %.Hao *et al.* [9] Conducted an experiment on boiling heat transfer characteristics inside a horizontal smooth tube of refrigerant-based nanofluid (R113-CuO) flow. The results show that the heat transfer coefficient increases to 29.7% using (0.15–1.5)% volume concentration. In the experimental investigation, Muhbubul *et al.* [10] investigated the thermal conductivity and viscosity of theAl_2O_3/R141b nanorefrigerant for volume concentrations. The results

showed that the viscosity and thermal conductivityof the Al_2O_3/R141b nanorefrigerant with volumefraction of 2 % are respectively 179 and 1.626 times greaterthan R141b.Kedzierski [11] studied the effect ofAl_2O_3-R134a pool boiling heat transfer. They found that for 0.5%nanolubricant mass fraction, the nanoparticles increase the heattransfer by as high as 400% for the lowest heat flux compared withthe heat transfer of pure R134a/polyolester (99.5/0.5). Kedzierski and Gong [12] studied the effect of CuO-R134a pool boiling heat transfer. They found that the nanoparticles increase the heat transfer by50–275% compared with the heat transfer of pure R134a/polyolester (99.5/0.5). Jiang *et al.* [13] measured the thermal conductivity of Four different types of CNTs with R113 refrigerant for volume concentrations of 0.2 to 1%. The authors modified the U-Choi model [14] and introduced a correlation to measure the thermal conductivity of CNT nanorefrigerants. Jiang *et al.* [15] investigated the thermal conductivity of R113 with Cu, Al, Ni, CuO and Al2O3 with controlled volume concentrations of 0.1 to 1.2%. The authors also developed a modified model based on the Wang model to measure the thermal conductivity of the nanorefrigerants.

Challenges

The applications of nanorefrigerants are seems very attractive due to potential characteristics. But to obtain efficient nanorefrigerant is very difficult task. Most of the time performance of nanorefrigerants kill by various factors such as poor stability, high pressure drop, high pumping power, low specific heat, particle settling, and high production cost.

Conclusions:

From above listed research reports, it is observed that the addition of nanoparticles leads to a better system performance and energy efficiency. Also, it is observed that thermos-physical properties are mainly depends on concentration of metal oxide impurity in based fluid that is nanorefrigerants. In addition to this shape and particle size of metal oxide nanoparticles are play important role in enhancement of thermo-physical properties of nanorefrigerants. But, optimization of these parameters is quite difficult. In addition to this, poor stability and high cost of preparation are still the great difficulties in development of nanorefrigerants.

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CHAPTER
16

OPEN MAPPING THEORM: AN APPLICATION OF BAIRE'S CATEGORY THEOREM

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Abstract:

In this chapter, our goal is to expound the importance of Baire's Category Theorem in mathematics. In achieve this goal; we study a very famous result of functional analysis, namely, the Open Mapping Theorem. The Open Mapping Theorem and Baire Category Theorem are foundational results in functional analysis, particularly related to the study of Banach spaces (complete normed vector spaces). The Open Mapping Theorem states that a surjective bounded linear operator between Banach spaces is an open map, meaning it maps open sets to open sets. This theorem's proof heavily relies on the Baire Category Theorem, which states that a complete metric space cannot be expressed as a countable union of nowhere dense sets.

1. Introduction:

In mathematics, the Baire's category theorem is an important tool in the study of complete spaces, such as Banach spaces and Hilbert spaces that arise in topology and functional analysis. In functional analysis, two of the most powerful theorems, the open mapping theorem and uniform boundedness principle are direct consequences of the Baire's category theorem. The principle of uniform boundedness by S. Banach and Hilbert Steinhaus (1927) is of great importance. In fact, throughout analysis there are many instances of results related to this principle, the earliest being an investigation by H. Lebesgue (1909). The principle of uniform boundedness is often regarded as one of the cornerstones of functional analysis in normed spaces, the others being the Hahn –Banach theorem, the open mapping theorem and the closed graph theorem. Unlike the Hahn – Banach theorem, other three of these four theorems require completeness. Indeed, they characterize some of the most important properties of Banach spaces which normed spaces in general may not have. But we obtain all three theorems from a common source, which is Baires category theorem. From the Baire's category theorem, we can derive the principle of

uniform boundedness and the open mapping theorem. On the other hand, the closed graph theorem is an application of the open mapping theorem.

2. Preliminaries:

The open mapping theorem will be concerned with open mappings. These are mappings such that the image of every open set is an open set (definition below). It is well known that open mappings are of general interest. As in the uniform boundedness theorem we again need completeness and present theorem exhibits another reason why Banach spaces are more satisfactory than incomplete normed spaces. The theorem also gives conditions under which the inverse of a bounded linear operator is bounded. The proof of the open mapping theorem is based on Baire's category theorem. To establish this result, we need a lemma and the proof of this lemma depends on Baire's category theorem.

Lemma 2.1: Let X and Y be two Banach spaces, and let $T: X \to Y$ be an onto continuous linear operator. If zero is an interior point of a subset A of X , then zero is also an interior point of $T(A)$.

Proof: Set $V = \{x \in X : \|x\| \leq 1\}$ and observe that $rV = \{rx : x \in V\}$ is the closed ball with center at zero and radius r. Since zero is assumed to be an interior point of A, there exists $r > 0$ with $rV \subseteq A$. By the linearity of T we must have $T(rV) = rT(V) \subseteq T(A)$. Hence to establish the result it is enough to show that zero is an interior point of $T(V)$.

Clearly, $X = \bigcup_{n=1}^{\infty} nV$ holds and since T is an onto linear operator, $Y = \bigcup_{n=1}^{\infty} nT(V)$ also holds. By Baire's category theorem, there exists some K such that $\overline{kT(V)}$ has a nonempty interior. Since $\overline{kT(V)} = k\overline{T(V)},$ it follows that $\overline{T(V)}$ has an interior point. That is, there exists some $y_0 \in \overline{T(V)}$ and $r > 0$ such that $B(y_0, 2r) \subseteq \overline{T(V)},$. Now if $y \in Y$ satisfies $\|y\| < 2r$, then $y - y_0 \in \overline{T(V)}$.

Therefore $y = (y - y_0) + y_0 \in \overline{T(V)} + \overline{T(V)} = 2\overline{T(V)},$

where the last inclusion follows from the identity $V + V = 2V$. That is,

$$\{y \in Y : \|y\| < r\} \subseteq 2\overline{T(V)}.$$

By the linearity of T, it follows that, $\{y \in Y : \|y\| < r2^{-n}\} \subseteq 2^{-n}\overline{T(V)} = \overline{T(2^{-n}V)}$

holds for each n.

Now let $y \in Y$ be fixed such that $\|y\| < r2^{-1}$.. Since $y \in \overline{T(2^{-1}V)}$, there exists some $x_1 \in 2^{-1}V$ such that $\|y - T(x_1)\| < r2^{-2}$. Now proceed inductively.

Assume that x_n has been selected such that $x_n \in 2^{-n}V$ and $\left\|y - \sum_{i=1}^{n} T(x_i)\right\| < r2^{-n-1}$..

Clearly $y - \sum_{i=1}^{n} T(x_i) \in \overline{T(2^{-n-1})V}$ and so there exists some $x_{n+1} \in 2^{-n-1}V$ with $\left\|y - \sum_{i=1}^{n+1} T(x_i)\right\| < r2^{-n-2}$. Thus, a sequence $\{x_n\}$ is selected such that $\|x_n\| \le 2^{-n}$ and $\left\|y - \sum_{i=1}^{n} T(x_i)\right\| = \left\|y - T(\sum_{i=1}^{n} x_i)\right\| < 2r^{-n-1}$ holds for all n.

Next define $s_n = x_1 + x_2 + ... + x_n$ for each n, and note that $\|s_{n+p} - s_n\| = \left\|\sum_{i=n+1}^{n+p} x_i\right\| \le \sum_{i=n+1}^{n+p} \|x_i\| \le 2^{-n}$ for all n and p shows that $\{s_n\}$ is a Cauchy sequence .Since X is Banach, so $\{s_n\}$ is convergent. Let $x = \lim s_n$ in X. Then $\|x\| \le \sum_{n=1}^{\infty} \|x_n\| \le 1$ (i.e $x \in V$) and by the continuity and linearity of T, we get $T(x) = \lim_{n\to\infty} T(s_n) = \lim \sum_{i=1}^{n} T(x_i) = y$.

That is, $y \in T(V)$, and so $\{y \in Y : \|y\| < \frac{r}{2}\} \subseteq T(V)$.The proof of the lemma is now complete.

Definition 2.2: Let X and Y be metric spaces. Then $f : X \to Y$ is called an open mapping if $f(A)$ is open in Y whenever A is open in X.

3.Main Theorem (Open Mapping Theorem):

Let X and Y be two Banach spaces, and let $T : X \to Y$ be a bounded linear operator .If T is onto, then T is an open mapping.

Proof: Let O be an open subset of X and let $y \in T(O)$. Pick a point $x \in O$ such that $y = T(x)$, and note that $y - T(O) = T(x - O)$ holds. Now observe that zero is an interior point of $x - O$ hence, by lemma 2.1, zero is also an interior point of $y - T(O) = T(x - O)$. This implies that y is an interior of $T(O)$. Since y is arbitrary, $T(O)$ is an open set, and the proof of the theorem is complete.

Remark: In addition T is one to one, then T is a homeomorphism. Because if T is one to one, then T will be a bijection and hence T^{-1} is exists. By open mapping theorem T is

open and hence T^{-1} is bounded as if M is open in X then $(T^{-1})^{-1}(M) = T(M)$ is open in Y. Thus if $T: X \to Y$, where X and Y are Banach spaces, is a bijection then T^{-1} is bounded and this result is known as **Bounded Inverse Theorem.**

Theorem 3.1. Let X be a linear vector space that is complete in each of the norms $\| \|_1$ and $\| \|_2$, and suppose that there is a constant c such that $\|x\|_1 \le c\|x\|_2$ for all $x \in X$. Then the norms are equivalent. That is, there is second constant c^1 such that $\|x\|_2 \le c^1\|x\|_1$ for all $x \in X$.

Proof: Consider the identity mapping $I: (X, \| \|_2) \to (X, \| \|_1)$. Clearly I is one to one and onto. Since $\|x\|_1 \le c\|x\|_2$ for all $x \in X$ so I is bounded. Again by open mapping theorem I is open. Hence I^{-1} is bounded. This implies that there exists some c^1 such that $\|x\|_2 \le c^1\|x\|_1$ for all $x \in X$.

Theorem 3.2: Let $T: X \to Y$ be a bounded linear operator where X and Y are Banach spaces. If T is bijective then there exists $a, b > 0$ such that $a\|x\| \le \|Tx\| \le b\|x\|$ for all $x \in X$

Proof: Since T is bounded so there exists $b > 0$ such that $\|Tx\| \le b\|x\|$ for all . $x \in X$ .....(1)

Since T is bijective, i.e. $T^{-1}: X \to Y$ exists and $TT^{-1} = I = T^{-1}T$.

Therefore by open mapping theorem, T^{-1} is bounded so there exists $\lambda > 0$ such that

$$\|T^{-1}y\| \le \lambda\|y\| \text{ for all } y \in Y$$

$$\Rightarrow \|T^{-1}T(x)\| \le \lambda\|y\|$$

$$\Rightarrow \|x\| \le \lambda\|Tx\| \text{ for all } x \in X$$

$$\Rightarrow \frac{1}{\lambda}\|x\| \le \|Tx\|$$

$$\Rightarrow a\|x\| \le \|Tx\| \text{ where } \frac{1}{\lambda} = a \text{ .....(2)}$$

Therefore (1), (2) $\Rightarrow a\|x\| \le \|Tx\| \le b\|x\|$ for all $x \in X$

This completes the proof.

We know that $C[0,1]$, the collection of all real valued continuous functions defined on $[0,1]$ is a vector space over R. Now we define two norms in $C[0,1]$ as

$$\|f\|_\infty = \sup\{|f(x)| : x \in [0,1]\} \text{ and}$$

$$\|f\|_1 = \int_0^1 |f(x)|dx \text{ for } f \in C[0,1].$$

Theorem 3.3: $(C[0,1], \|f\|_\infty)$ is a Banach space.

Proof: See page 35, example 5.16 in [2].

Theorem 3.4: $(C[0,1], \| \|_1)$ is not a Banach space.

Proof: Define the identity operator $I : (C[0,1], \| \|_\infty) \to (C[0,1], \| \|_1)$

Then $\|I\| = \sup\{\|I(f)\|_1 : \|f\|_\infty = 1, f \in C[0,1]\}$

Now $\|I(f)\|_1 = \|f\|_1 = \int_0^1 |f(x)dx| \le \|f\|_\infty$ so $\|I\| \le 1$.

Also $f(x) = 1$ for all $x \in [0,1]$ is a continuous function and $\|f\|_\infty = 1$, so $\|I\| = 1$.

Hence I is bounded, i.e., continuous operator.

Again consider the identity operator $I^{-1} : (C[0,1], \| \|_1) \to (C[0,1], \| \|_\infty)$.

Define $f_n(x) = (n+1)x^n$ for each n

Then $$\|f_n\|_1 = \int_0^1 |(n+1)x^n| dx = \int_0^1 (n+1)x^n dx = 1$$

Also $\|f_n\|_\infty = n+1$ Now $\|I^{-1}\| = \sup\{\|I^{-1}(f)\|_\infty : \|f\|_1 = 1\}$

$$\ge \sup\{\|I^{-1}(f_n)\|_\infty\}$$

$$= \sup\{\|f_n\|_\infty\}$$

$$= \sup\{n+1 : n \in N\}$$

$$= \infty$$

Hence I^{-1} is bounded and therefore I is not open. But I is bounded, onto. Therefore by open mapping theorem either $(C[0,1], \|f\|_\infty)$ or $(C[0,1], \| \|_1)$ is not Banach. But by theorem 3.3 $(C[0,1], \|f\|_\infty)$ is a Banach space. Hence $(C[0,1], \| \|_1)$ is not Banach.

In connection with the openness property of a linear map, the following result is useful.

Proposition 3.5: Let T be a bounded linear map from a normed linear space X on to a normed linear space Y.Then T is open if and only if there is $\lambda > 0$ such that for each $y \in Y$, there is $x \in X$ where $T(x) = y$ and $\|x\| \le \lambda \|y\|$.

Remark: The above result enables us to obtain a partial converse of the open mapping theorem.

Theorem 3.6: Let X and Y be Banach spaces. Then the set of all surjective maps in $L(X,Y)$ is open in $L(X,Y)$.

Proof: Let T be a surjective map in $L(X,Y)$. Let $U \in L(X,Y)$ and $\|T-U\| < \frac{1}{2^k},$ where k is a real number with the property as in above proposition. We have prove that U is surjective.

Let $y \in Y$ and $\|y\| \le 1$, it follows from above proposition that there exists $x \in X$ such that $T(x) = y$ and $\|x\| \le k$. Let $y_1 = T(x) - U(x).$ Then $\|y_1\| \le \frac{1}{2}$ and there exists $x_1 \in X$ such that $T(x_1) = y_1$ and $\|x_1\| \le \frac{k}{2}$ .Let $y_2 = T(x_1) - U(x_1).$then $\|y_2\| \le \frac{1}{2^2}$. Continuing inductively, we can find x_n such that $T(x_n) = y_n$ and $y_{n+1} = T(x_n) - U(x_n)$

$$\|y_n\| \le \frac{1}{2^n}, \qquad \|x_n\| \le \frac{k}{2^n}$$

It then follows that $y = U(x) + U(x_1) + ... + U(x_n).$

Thus $U(z) = y$ where $z = \sum_{n=1}^{\infty} x_n$. This proves the theorem.

Now we move to another consequence of open mapping theorem. i.e. Open mapping theorem is used in Factor spaces. The results on factor spaces and direct sums represent important auxiliary tools for the investigation of linear and nonlinear operator equations.

But to show this, we need some definitions.

Let L be a linear subspace of the linear space X over K. For all $u, v \in X$, we define

$$u \equiv v (\mathrm{mod}\, L) \text{ iff } u - v \in L \text{.....} \text{.....} \text{.....} (1)$$

This is an equivalence relation. In fact, for all $u, v, w, z \in X$ and $\alpha \in K$, we have the following

$$u \equiv v (\mathrm{mod}\, L)$$

$$u \equiv v (\mathrm{mod}\, L) \Rightarrow v \equiv u (\mathrm{mod}\, L)$$

$$u \equiv v (\mathrm{mod}\, L),\ v \equiv w (\mathrm{mod}\, L) \Rightarrow u \equiv w (\mathrm{mod}\, L)$$

This equivalence relation is compatible with the linear structure of L :

$$u \equiv v (\mathrm{mod}\, L) \Rightarrow \alpha u = \alpha v (\mathrm{mod}\, L) \text{ .....} (2)$$

$u \equiv w(\text{mod}L)$, $v \equiv z(\text{mod}L) \Rightarrow u + v \equiv w + z(\text{mod}L)$

Definition 3.7: The factor space X/L consists of all the equivalence classes $[u]$ with respect to (1), that is $v \in [u]$ iff $u \equiv v(\text{mod}L)$. Explicitly, this means that $[u] = u + L$

The elements v of the class $[u]$ are called the representatives of $[u]$. Obviously $[u] = [v] \Leftrightarrow u \equiv v(\text{mod}L)$ .....(3)

If we introduce the linear operations $\alpha[u] = [\alpha u]$

$$[u] + [v] = [u + v] \text{.....} \text{.....} (4)$$

the factor space X/L becomes a linear space. The operations in (4) are well defined namely; they are independent of the chosen representatives. This follows from (2) and (3). For example, if $[u] = [v]$ then $u \equiv v(\text{mod}L)$ and hence $\alpha[u] = [\alpha u](\text{mod}L)$ that is $[\alpha u] = [\alpha v]$.

In other words, the factor space X/L consists of all the different sets $u + L$ where $u \in X$ and linear operations on X/L are given through $(u + L) + (v + L) = (u + v) + L$ and $\alpha(u + L) = \alpha u + L$ which corresponds to the usual operations $A + B$ and αA for subsets A and B of linear spaces.

Proposition 3.8: Let L be a closed linear subspace of the normed space X over K.Then the following are true.

(1) The factor space X/L becomes a normed space over K with respect to the norm $\|[u]\| = \inf_{v \in [u]} \|v\|$

(2) If X is a Banach space then so is X/L

Since $[u] = u + L$ we get $\|[u]\| = dist(0, u + L) = dist(u, L)$

Definition 3.9: Let L be a linear subspace of the linear space X over K. Then the canonical mapping $\Pi : X \to X/L$ is defined through $\Pi(u) = [u]$ for all $u \in X$ where $[u] = u + L$

Proposition 3.10: If L is a closed linear subspace of the normed space X over K, then the canonical mapping $\Pi : X \to X/L$ is linear, continuous and surjective.

Proof: See page 187 in [10].

Remark: Let $A: X \to Y$ be a linear continuous operator, where X and Y are Banach spaces over K. We define the operator $[A]: X/N(A) \to R(A)$ .....(A) through $[A][u] = Au$.

This definition is independent of the selected representatives. In fact let $[u] = [v]$. Then $u - v \in N(A)$ that is $A(u - v) = 0$ and hence $Au = Av$

Proposition 3.11: Let the range $R(A)$ of the operator A be closed.

(1) The operator $[A]$ from (A) ids a linear homeomorphism.

(2) There exists a number $c > 0$ such that

$c..dist(u, N(A)) \le \|Au\|$ for all $u \in X$

Proof (1) : The null space $N(A) = \{u \in X : Au = 0\}$ is closed. In fact, if $Au_n = 0$ and $u_n \to u$ as $n \to \infty$ then $Au = 0$. Thus $X/N(A)$ is Banach space. Obviously, the operator $[A]$ is linear. Since $\|[A][u]\| = \|Av\| \le \|A\|\|v\|$ for all $v \in [u]$

We have $\|[A][u]\| \le \|A\|\|[u]\|$ and thus $[A]$ is continuous.

Furthermore, the operator $[A]$ is bijective. Infact, if $[A][u] = 0$ then $u \in N(A)$ and hence $[u] = 0$.

Since $R(A)$ is closed linear subspace of the Banach space Y the range $R(A)$ is also Banach space. The Bounded inverse theorem tells us that the inverse operator $[A]^{-1} : R(A) \to X/N(A)$ is continuous.

(2) By (1) there is a constant $d > 0$ such that $\|[A]^{-1}[u]\| \le d\|[u]\|$ for all $[u] \in X/N(A)$. Hence $\|[v]\| \le d\|[A][v]\|$ for all $[v] \in X/N(A)$.

Hence (2) where $c = d^{-1}$

Now move to direct sum and projections- where Bounded inverse theorem is used.

Definition 3.12: Let X be linear space over K and let L_1 and L_2 be linear subspaces of X .

(1) We write $X = L_1 \oplus L_3$ iff each $u \in X$ allows the following unique representation:

$u = u_1 + u_3$ where $u_1 \in L_1$ and $u_2 \in L_2$ .....(B)

We say that X is the direct sum of L_1 and L_2 and that L_2 is an algebraic complement of L_1 in X .

(2) The operator $p: X \to X$ is called an algebraic projection iff p is linear and $p^2 = p$

(3) If X is normed space, then the operator $p: X \to X$ is called an continuous projection iff p is a continuous algebraic projection. Obviously $X = L_1 \oplus L_3$ iff $X = L_2 \oplus L_1$. Moreover, let $X = L_1 \oplus L_3$, then $u \in L_1 \cap L_2$ implies $u = 0$.

This follows from $u = u + 0 = 0 + u$ and from the uniqueness of the decomposition in (B).

Now if we consider the linear operator equation $Au = b$, $u \in X$. Then we have the following theorem—

Theorem 3.13: Supposed that the operator $A: X \to X$ is linear, where X and Y are linear spaces over K. Let L bee any fixed algebraic complement of the null space $N(A)$, namely L is a linear subspace of X such that $X = N(A) \oplus L$ .....(**)

Then the following statements are true.

(1) The restriction $A: L \to R(A)$ is linear and bijective. Hence codim $N(A) =$ dim $R(A)$

(2) In addition, suppose that X and Y are Banach spaces L and $R(A)$ are closed, and the operator $A: X \to Y$ is continuous. Then the operator from (c) is a linear homomorphism.

[Since $R(A) = A(X)$. The number dim $R(A)$ is called the rank of A. We denote this as rank A =dim $R(A)$]

Proof: (1) It follows from $Au = 0$ with $u \in L$ that $u \in N(A) \cap L$. Hence $u = 0$ by (**).

(2) This follows from the Bounded inverse theorem.

Theorem 3.14: Let X and Y are Banach spaces and $F: X \to Y$ be a one to one bounded linear map. Then its range $R(F)$ is closed in Y iff $F^{-1}: R(F) \to X$ is bounded.

Proof: Let $Y_1 = R(F)$ be closed in Y. Then $Y_1 = R(F)$ is Banach, since Y is Banach. Moreover $F: X \to Y_1$ is a bijective bounded linear map and X is Banach. Therefore the Bounded inverse theorem gives the continuity of F^{-1}

Theorem 3.15: Suppose X is a Banach space, A and B are closed subspaces of X and $A + B = X$. There exists a constant $\gamma < \infty$ such that every $x \in X$ has a representation $x = a + b$, where $a \in A$, $b \in B$ and $\|a\| + \|b\| \le \gamma \|x\|$.

Proof: Let Y be the vector space of al ordered pairs (a,b) with $a \in A$, $b \in B$ and component wise addition and scaler multiplication, normed by $\|(a,b)\| = \|a\| + \|b\|$

Since A and B are complete, Y is Banach space. The mapping $\Lambda : Y \to X$ defined by $\Lambda(a,b) = a + b$ is continuous, since $\|a+b\| \le \|(a,b)\|$ and maps Y onto X. By the open mapping theorem, there exists $\gamma < \infty$ such that each $x \in X$ is $\Lambda(a,b)$ for some (a,b) with $\|(a,b)\| \le \gamma \|x\|$.

Theorem 3.16: Let X be separable Banach space. Then there exists a closed linear subspace L of the sequence space l_1 such that X is topologically isomorphic to the quotient space l_1 / L

Proof: Let $\{x_n\}$ be a dense sequence in X. Define the mapping $T : l_1 \to X$ by $T(y) = \sum a_n x_n$, $y = \{a_n\}_{n=1}^{\infty}$.

Clearly $\|T(y)\| \le \|y\|$ Let $L = T^{-1}\{0\}$. Define now the mapping τ by $\tau(y + L) = T(y)$. This map is well defined and is continuous, linear, one to one mapping from l_1 / L into X. If T is surjective, then τ is surjective. By applying the open mapping theorem the proof will be complete in this case. Then it is sufficient to prove that T is surjective. Let $x \in X$ and $\|x\| < 1$. Choose x_{n_0} such that $\|x - x_{n_0}\| < \frac{1}{2}$ then choose $n_1 > n_0$ such that $\|2(x - x_{n_0}) - x_{n_1}\| < \frac{1}{2}$.

Arguing inductively, we can finds subsequence $\{x_{n_k}\}$ such that $x = \sum_{k=0}^{\infty} \frac{x_{n_k}}{2^k}$.

Let $y = \{a_j\}$ be defined so that $a_j = \frac{1}{2^i}$ if $j = n_i$

$= 0$ if $j \ne n_i$ all i

Then $y \in l_1$ and $T(y) = x$. This shows that T is surjective.

Now we can mention an application of the open mapping theorem to obtain result about perturbations in different equations.

Example 3.17: Consider the differential equation, $x''(t) + a_1(t)x'(t) + a_2(t)x(t) = y(t)$ .....(*)

Here a_1, a_2 and y are members of $C[a,b]$. An initial value problem (For details see ordinary differential equation by Coddington) for (*) calls for finding a twice continuously

differential function x on $[a,b]$ satisfying (*) and satisfying the initial conditions $x(a) = x'(a) = 0$

A standard theorem in differential equations asserts that this initial value problem has a unique solution. We wish to study the dependency of the function x on y and vice-versa.

Let $X = C^2$, the space of twice continuously differential functions. Then X becomes a Banach space under the norm $\|x\| = \max\{\|x\|_\infty, \|x'\|_\infty, \|x''\|_\infty\}$ where $\| \ \|_\infty$ denotes the usual supremum norm in $C[a,b]$. Let $Y = C[a,b]$. Let $T: X \to Y$ be defined by $Tx = y$ where $x''(t) + a_1(t)x'(t) + a_2(t)x(t) = y(t)$. The standard theorem in differential equations that we mention before asserts that T is one to one on X and maps X onto Y. We show that T is a continuous operator.

Let $A = 1 + \|a_1\|_\infty + \|a_2\|_\infty$. Then $\|Tx\|_\infty = \|y\|_\infty \le \|x''\|_\infty + \|a_1\|_\infty \|x'\|_\infty + \|a_2\|_\infty \|x\|_\infty \le A\|x\|$ so T is a continuous. By the open mapping theorem, T^{-1} is also continuous. We can interpret this as saying that small perturbations of the function y will result in small perturbations of the solution $x \in C^2$. This means that such a perturbed solution x_1 will be 'C^2-close' to x, that is, x_1, x_1' and x_1'' will be (uniformly) close to x, x' and x'' respectively.

Conclusion:

Here, the open mapping theorem exhibits the reason why Banach spaces are more satisfactory than incomplete normed spaces. The theorem also gives conditions under which the inverse of a bounded linear operator is bounded. Moreover, Bounded Inverse theorem has shown that just as the inverse of a bijective linear map from a linear space to a linear space is linear and the inverse of a bijective closed map from a metric space to a metric space is closed, the inverse of a bijective, linear and continuous map from a Banach space to a Banach space is linear and continuous. The theorem 4, have shown that open mapping theorem can be used to obtain a theorem showing how to check that two norms on Banach space are equivalent.

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