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PLANT VIRUSES NANOTECHNOLOGY

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Abstract: This article is a summary of recent achievements in "Plant Virus Nanoparticles." Viruses, serve as inventive minuscule frameworks, which are crucial for nanotechnology and have various applications. Some of the main benefits of viruses over artificially coded nanomaterials are the well-defined and simple physical arrangement of their units into different shapes and sizes. The review begins by examining the large variety of existing as well as the various strategies for creating plant virus-based nanoparticles and the engineering techniques that are used to add more functionality. The review also discusses various applications and outcomes of plant virus-based products in healthcare and biotechnology industries. Advances in the sensible planning of plant virus based nanostructures will continue to strengthen and expand this discipline, opening up exciting new opportunities. Nanotechnology applications include nanoparticle-interceded quality or DNA movement in plants for bug-free assortments, food handling, and storage, and extended item usefulness durations. Biomass-to-fuel output could be increased through nanotechnology.

Index Terms **- Plant-made pharmaceuticals (PMPs); Nanotechnology; virus; immune system; vaccine.**

I. INTRODUCTION

Nanoscale design is reshaping science and design in a different ways. Particularly through the use of viral platforms, science has advanced in the gathering and creation of novel materials with a broad spectrum of purposes. (Wen & Steinmetz - Chemical Society Reviews - 2016). Before studying specific plant infections' nanoparticles and antibodies applications utilizing nanotechnology in the pharmaceutical field, it is perhaps appropriate to first consider what is meant by the term 'nanotechnology,' considering that the true sizes of the materials are in question, with some believing the appropriate size ranges between 1 and 100 nanometers, rather than just under 1 micron (1000 nanometers). Indeed, when the plant writing is examined, it is discovered that some include nanoparticles, even though the sizes are clearly in the micron range. (Chapman - Expert Opinion on Therapeutic Patents - 2005)

Synthetic biology and chemistry innovations have had an impact on a variety of scientific, commercial, and medical domains by making it possible to produce nanoscale devices with increasingly regulated designs. Even still, wide-scale manufacture of material is complex, and preparing structurally uniform populations of particles is tough. Bio nanomaterials based on viruses, on the other hand, enable template-guided synthesis of millions of similar nanomaterials in living cells. (Koudelka et al. - Annual Review of Virology - 2015) Viruses infect bacteria, humans, and plants, and they can be employed to create virus based nanoparticles (VNPs). Viruses are an excellent place to start as they are evolved to distribute nucleic acids naturally and thus can be manipulated to deliver other compounds such as medications and imaging techniques. Further, viruses have a high rate of replication, enabling the mass production of VNPs at a low cost. (Koudelka et al. - Annual Review of Virology - 2015)

Viral nano-particles (VNPs) have recently attracted a lot of interest as a new type of nanocarrier for biomedical applications. (Barrett - npj Vaccines - 2016) These are viable substitutes for synthetic nanoparticles due to their biocompatible and biodegradabe nature, and are simple to produce and regulate for quality. Plant viruses have appeared as interesting tools for usage as nanomaterials in biotechnological applications. Plant viruses differ from manufactured nanomaterials in terms of stability, adaptability, shape and size diversity for medicine administration, and the harmless properties of plant viruses in human beings. They are replication-deficient, empty, genetically-sterile capsids. (Ridgway & Taylor - Basic Science in Obstetrics and Gynaecology - 2010) VLPs with nanoparticle-like behavior can be used to encapsulate therapeutic substances inside capsids for a range of imaging and drug-delivery applications. (Shoeb et al. - Vaccines - 2021)

Plant infection-based viral nanoparticles can obstruct the movement of various tumors, further showing their general potential in medicine. (Yusibov et al. - Human Vaccines - 2011),(Yusibov et al. - Human Vaccines - 2011) All immunizations can be divided into different types, such as antibodies against immune system disorders, vaccinations against cancer, and antibodies against incurable diseases. (Balke & Zeltins - Viruses - 2020)

II. VIRUS STRUCTURES

Viruses have complicated head-to-tail arrangements, icosahedral and helical symmetries, and occur in a variety of shapes and sizes. Inorder to spread to other cells and human beings, release of the pathogenic virus particle from the host cell is required. During the procedure, the virus's DNA genome, either ds- DNA, ss- DNA, ds- RNA, or ss- RNA, must be protected. Proteins that can degrade or break down nucleic acid in the extracellular environment pose a threat to the structural integrity of the virus. The nucleic acid strands can also break under the influence of physical stimuli like the flow of fluids or air. (Louten - Essential Human Virology - 2016) The virus covers its sensitive nucleic acid in a covering of protein known as the capsid to protect it from the hostile environment. Similar to the bricks in a wall, the proteins that make up the capsid can be of a variety of kinds and are repeated sequentially to form the entire capsid. The nucleic acid inside the capsid is adequately protected and is physically challenging to break free. The nucleocapsid of the virion is composed of both the nucleic acid and the capsid. The capsid of most viruses is encased in an envelope. (Louten - Essential Human Virology - 2016)

Plant viruses are non-enveloped with genomes made up of one or more positive-sense RNA strands. Similar to all viruses, these particles are composed of highly repeated patterns of protein parts that come together around the genome to form enormous, well-organized macromolecular structures. (Steele et al. - WIREs Nanomedicine and Nanobiotechnology - 2017)

III. TYPES OF VIRUSES

Based on their symmetry, viruses can be classified into helical and icosahedral. (Strable et al. - Bioconjugate Chemistry - 2008)

Helical/ Rod-shaped viruses include:

- Tobacco mosaic virus (TMV)
- Potato virus X (PVX)

Icosahedral shapes include:

- Cowpea mosaic virus (CPMV)
- Cowpea chlorotic mottle virus (CCMV). (Venkataraman et al. - Frontiers in Bioengineering and Biotechnology - 2021)

IV. PROCESS OF VIRUS EXPRESSION

Viruses have been built to protect and transport their nucleic acid payload, therefore they can resist stressful conditions and are stable for long periods. Viral capsids can be internally and externally modified and are capable of encapsulation of sensitive chemicals as well as displaying moieties on the surface (Wen & Steinmetz - Chemical Society Reviews - 2016),(King et al. - Nature - 2014) Genetic modification, bio-conjugation, infusion, bio-mineralization, and self-assembly are among the most commonly employed methods. (Wen & Steinmetz - Chemical Society Reviews - 2016)

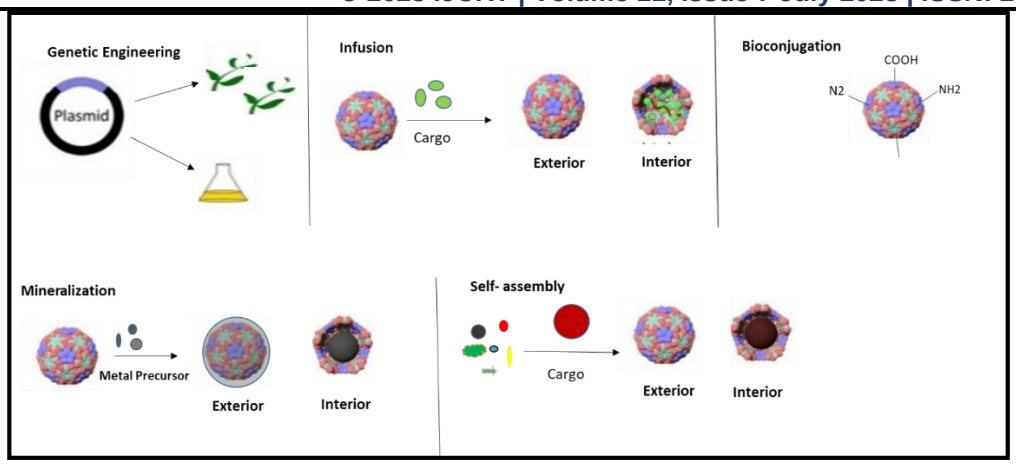

Fig: 2 Process of Virus Expression

1. Genetic modification:

The genetic coding of VNPs determines the outer proteins that are produced by the virus. Because virus nucleic acid sequences are generally short, numerous virus genomes have been decoded and reported. Inserting or replacing residues to add functional groups can be done by genetic engineering, as cysteine mutants are the most well-known due to the presence of di- sulfide bonds, in connection with gold, and bio-conjugation with thiol- selective chemicals. (Altintoprak et al. - nano Online - 2016),(Wang et al. - Chemistry & Biology - 2002) Foreign amino acids can also be inserted, for more altered chemical changes. Additionally, residue can be removed from the coat protein leaving behind a single unique reactive site. Larger modifications, such as the addition of purification tags, are also possible. (Strable et al. - Bioconjugate Chemistry - 2008),(Chatterji et al. - Nano Letters - 2005)

2. Bioconjugation:

Conjugation techniques that target natural and artificial amino acids present in virus capsids permit a wide range of alterations. Many viruses are chemically altered in internal and external areas. Protein lysine, cysteine, aspartic acid, glutamic acid, and residues of tyrosine are some of the most commonly altered groups which can be customized and can undergo bio-conjugation reactions of N-hydroxy succinimide (NHS) ester conjugation, carbo-di-imide activation, Michael addition, and azo coupling chemistries. (Chen et al. - Biomineralization Forming Process and Bio-inspired Nanomaterials for Biomedical Application: A Review - 2019) Replacing homocysteine residues with homo-propargyl - glycine (HPG) or azido-homo-alanine (AHA) remaining to add alkyne or azide functions, respectively, are some alternatives to these organic amino acids. (Strable et al. - Bioconjugate Chemistry - 2008),(Schlick et al. - Journal of the American Chemical Society - 2005) Another novel strategy uses mutant t-RNA synthetases to link artificial amino acids to amber suppressor t-RNAs such that these amino acids can be integrated at the amber-stop codon locations. (Bruckman et al. - ChemBioChem - 2008)O-methyltyrosine, p-azido phenylalanine, p-acetyl phenylalanine, p-benzoyl phenyl-alanine, 3-(2-naphthyl) alanine, and p- amino phenylalanine are among the amino acids absorbed in this fashion. Because they provide azide and amine groups for specific coupling processes, p-azido phenylalanine, and pAF are particularly notable. (Prasuhn, Jr. et al. - Chem. Commun. - 2007)

3. Infusion:

Viruses are often flexible, with holes allowing tiny compounds like medicines and contrast agents to diffuse within and outside the capsid. The molecules may then be kept inside the capsid through interactions with the internal polymer-conjugated nucleic acid, electrostatic and/or affinity contacts with the nucleic acid within the shell, and/or interactions. (Hovlid et al. - ACS Nano - 2014), (Cao et al. - ACS Applied Materials & amp; Interfaces - 2015) Structural modification can be carried out by encapsulation of the drug particles by utilising pH or metal ion concentration. The gating process helps molecules diffuse into the particle when the capsid is in a swollen, open shape and when the pores are closed by changing the buffer conditions. The molecules of interest may either remain encapsulated

within the particles or gradually release them, depending on how the delivery mechanism is built. (Mao et al. - Science - 2004)

4. Bio-mineralization:

During the bio-mineralization process, viral particles with unique sizes and form control can serve as templates. Prerequisite metal ion nucleation and consequent shape-constrained beneficiation can be accomplished by modifying electrostatics or via mineralization-directing peptides. In order to find peptide nucleators and connectors that were extremely selective against a range of substrates, phage display such as zinc sulphide (ZnS) and gallium arsenide (GaAs) can be used. (Altintoprak et al. - nano Online - 2016)

It has been demonstrated that particles' interior and exterior structures, as well as icosahedral and rod-shaped viruses, all mineralize. The resultant hybrid inorganic-organic materials have a wide range of applications, varying from energy implementation as semiconductors to medical applications as contrast agents. (Dixit et al. - Nano Letters - 2006) The application primarily directs drug engineering, enzyme development, three-dimensional (3D) printing engineering, cancer engineering, bone engineering, and microbial engineering. (Gera et al. -Application of pulsed laser ablation (PLA) for the size reduction of non-steroidal anti-inflammatory drugs - 2020)

5. Self-assembly:

These virus-based particles function as full, reusable scaffolding. They can also be broken down and re-organised using either their own genomes or those of other organisms. Quantum dots, photosensitizer medicines, and gold nanoparticles are among the types of cargo that can be held by self-association. (Daniel et al. - ACS Nano - 2010) Adequate foreign cargo encapsulation is achieved with a decreased surface charge. Because of its effect on the curvature radius, cargo size affects assembly, and different cargo sizes can cause alteration in the capsid's shape and physical features of the capsid. (Mullard - Nature Reviews Drug Discovery - 2015)

V. METHODS FOR SYNTHESIS

A] Physical Methods:

1) Pulse laser ablation:

The process of removing material from a solid (or liquid) surface by subjecting it to a laser beam is referred to as laser ablation, also known as photoablation. (Brittain et al. - Biomedical Optics Express - 2022) The substance is heated by the absorbed laser energy at low laser flux and evaporates or sublimates. The material regularly changes into plasma at high laser flux. In contrast to comparatively long laser pulses, such as nanosecond pulses, which can heat, thermally change, or damage the processed material, ultrashort laser pulses process materials with minimal material damage.

Second Harmonic Generation (ND: YAG) type laser is for the most part utilized. Kind of laser, number of heartbeats, beating time, and sort of dissolvable where a chelating agent known to dissolve calcite, ethylenediaminetetraacetic acid (EDTA) influence the created nanoparticles. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (Zhou et al. - Journal of the American Chemical Society - 2010)

2) Mechanochemical synthetic combination:

One of the most important current approaches for producing nanomaterials is mechanochemical synthesis. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) Chemical and mechanical events are combined on a molecular scale in mechanochemical synthesis, a materials processing technology. By using only mechanical action (high pressure and mechanical tension between reactants and balls), a desired product can be produced at room temperature or at temperatures lower than those needed for conventional solid-state synthesis. The features of the final material can be changed by adjusting the milling time, powder-to-ball weight ratio, humidity, number, the atmosphere, milling gas pressure, and other

test factors. Numerous products, such as metastable phases, high-pressure phases, and unstructured and disordered phases, which might lead to the formation of novel materials, can be produced depending on the synthesis conditions. Mechanical energy is used to activate the synthetic response. Through reasonable dissolvable washing, the nanoparticles are recovered. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (El-Eskandarany - Mechanical Alloying - 2015)

3) Phase vapour deposition:

For a long time, vapour deposition techniques have been utilized to produce various materials such as fibers, nanotubes, thin films, powders, multilayer coatings, and graded composition deposits. Thin films have been made from a variety of sophisticated materials, including nano-crystalline and amorphous alloys, with thicknesses ranging from a few nanometers to thousands of nanometers. PVD and CVD are two methods for generating thin films using vapour deposition technology. Molecule size and their appropriation rely on the pace of vanishing and tension of gases. Metal compounds can be framed by utilizing responsive gases like O_2, H_2, and NH_3. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (Rane et al. - Synthesis of Inorganic Nanomaterials - 2018)

4) High ball processing technique:

A powder combination placed in a ball mill is subjected to high-energy collisions from the balls in a high-energy ball milling process. Traditional powder metallurgy methods fail to produce thin, equally dispersed oxide particles in nickel-base superalloys, but high-energy ball milling sometimes referred to as mechanical alloying, can achieve this. High-energy ball milling modifies the environment in which chemical reactions normally occur by altering the reactivity of as-milled particles or triggering chemical reactions during milling.
Planetary, vibratory, bar, tumbler mixers, and so on are ordinarily utilized for the union of nanoparticles. Type of plant, processing speed, time, temperature, endless size dispersion, and so on influence execution. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (Kumar & Mishra - Pramana - 2010)

5) Pulsed wire release technique:

The pulsed wire method quickly and precisely examines the first and second field integrals of undulators used in synchrotron light sources and free-electron lasers. Metal, oxide, and nitride nanoparticles are made utilizing this technique with High energy efficiency and creation rate. (Qiao et al. - Modern Inorganic Synthetic Chemistry - 2017)

B] Chemical Methods:

[1] Sonochemical strategy:

High-frequency ultrasound (20 kHz–10 MHz) is used to cause chemical reactions in molecules in the field of research known as sonochemistry. The sonochemical reaction is brought on by a physical phenomenon called acoustic cavitation. Simple, all-encompassing working conditions, and an example of regulating nanoparticle size. Formerly suggested for organizing iron nanoparticles, but currently used for many metals and metal oxides. (Cele - Engineered Nanomaterials - Health and Safety - 2020)

[2] Microemulsions:

Because the second reactant is diffusing into the droplets containing the reactant in the used micro-emulsion, the one-micro emulsion technique is usually driven by a diffusion-based process. The second frequently used method for producing nanoparticles is the two micro-emulsion operations. The amount of water, oil, and surfactant phases affects how many total nanoparticles are calculated. Surfactant summaries can range in size from 1 nm to 100 nm. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018)

[3] Electrochemical strategy:

The electrochemical cycle used involved a metallic anode dissolving in an aprotic solution. Anodically soluble silver ions were electro-reduced in acetonitrile-containing tetrabutylammonium to produce silver nanoparticles with sizes ranging from 2- 7 nm. It was possible to estimate the particle size by varying the current density. Using a variety of counter electrodes, it was determined how different electrochemical parameters affected the final particle size. The UV-Vis spectra revealed two distinct silver complexes. (Li et al. - Journal of Nanomaterials - 2011) The driving or controlling force is known as power. The plan is straightforward, environmentally friendly, cost-effective, highly adjustable, and so on.

C] Biological Methods:

1) By Microorganisms:

Metal ions are trapped on the surface or inside microbial cells, which allows microorganisms to synthesize nanoparticles. The trapped metal ions are transformed into nanoparticles in the presence of enzymes. Microorganisms change the solution's composition to make it supersaturated or more supersaturated than it was previously. Also, microorganisms may influence mineral formation by producing organic polymers, which can influence nucleation by promoting or inhibiting the stability of the earliest mineral seedsMetallic nanoparticles, oxide nanoparticles, and sulfide nanoparticles can be obtained by utilizing this strategy. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) Applications of nanoparticles by microorganisms are antibacterial specialists, biosensors, response rates enhancers, and so forth. (Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (Mittal et al. - Biotechnology Advances - 2013)

2) Using Plant Extracts:

Plant extracts are combined with the metal salt solution at room temperature to create nanoparticles. The reaction is completed in a short interval of time. This technique has been used to create titanium dioxide and silver nanoparticles. It may also be used to synthesize silver, gold, copper, and cadmium sulfide nanoparticles, among other materials. Applications include cytotoxicity, antimicrobial, reactant, luminescence, etc.(Gennari & Andrade-Gamboa - Emerging Materials for Energy Conversion and Storage - 2018) , (45)

VI. APPLICATIONS

[1] Medical care:

Viruses have long been used in healthcare for analytical and treatment purposes, and many more are currently being tested in clinical trials for monotherapy and as gene therapy vectors. Because bacteriophages and plant viruses do not multiply in mammalian cells, they are particularly appealing tools for biomedical applications. DNA can be found using the biomineralization-assisted amplification (BMA) approach. (Hwang et al. - ACS Applied Materials & Interfaces - 2013) This novel method can be used for producing crystalline calcium phosphate nanocomposite (ACP-NC), where an internal enzyme is used to control biomineralization processes. (Lustig & Levine - Journal of Virology - 1992) As a result, these platforms are expected to provide an additional layer of safety. (Wen et al. - Journal of Biological Physics - 2013) , (Flenniken et al. - Chemistry & Biology - 2006)

[2] Nanomedical viral engineering design :

Charge, shape, and surface ligand presentation are all key factors to consider when designing viruses for in vivo applications. These design characteristics influence their cellular interactions and tissue selectivity, as well as their circulation in the body. Some of the parameters (ligands over Charge (positive or negative), form and size (variable aspect ratio fibres and diameter spheres), preserving (self-proteins/peptides and polymer compounds of different dimensions and densities), and targeting are examples of receptors or environmental factors that appear on

different linkers and at different densities. When virus-based particles have a negatively charged surface, there seems to be a trend toward shorter circulation times. We discover the less than ten-minute circulation half-lives of negatively charged Cucumber mosaic virus (CCMV), Cowpea mosaic virus (CPMV), and Tobacco mosaic virus (TMV). (Bruckman et al. - Virology - 2014) , (Riedel - Baylor University Medical Center Proceedings - 2005)

[3] Imaging:

Plant viruses derived from the carnivorous plant Sarracenia purpurea for smallpox infection have been used in retinal imaging, axial magnetic resonance imaging (MRI), and positron emission tomography (PET) for tissue-specific imaging and contrast agent delivery (PET). The variety of ways for altering the particles, as well as proper assembly, make viruses useful as imaging probes. Furthermore, to prevent toxicity brought on by contrast agent tissue retention, evacuation and elimination from the body are crucial. Many VNP platforms are swiftly eliminated from the body (half-life of minutes). in contrast to some synthetic materials, like carbon nanotubes, gold, and silica, which take months to clear. Diagnostic imaging, as well as visualization of illness location and development, as well as therapy success, is a key tool in medicine. (Friedmann & Roblin - Science - 1972)

[4] Vaccines and immunotherapy:

Dmitry Ivanovsky and Martinus Beijerinck filtered TMV from plant sap and demonstrated its infectivity and replication. (Plotkin - Nature Medicine - 2005) Safer vaccination substitutes, such as attenuated viruses, deactivated or subunit viruses, inert infectious VLPs, nanoparticle shipment, and nucleic acid vaccines, have since been developed in place of live viruses. (Friedmann & Roblin - Science - 1972) Vaccines have been developed for a variety of diseases like polio and measles, yet vaccines against HIV and other alarming diseases are not available. (Fontana et al. - Small - 2014)

[5] Gene delivery:

In addition to vaccines, full-length DNA, tiny intervening RNAs, and genome-editing instruments like nucleases have all been delivered by viruses to treat a range of disorders. (Lin et al. - Acta Biomaterialia - 2008) This concept of gene delivery has a lengthy history, having been first put forth more than 40 years ago. Since then, a lot of work has gone into developing gene therapy to cure a variety of illnesses, including cancer, Parkinson's condition, cystic fibrosis, and haemophilia, to mention a few. (Lin et al. - Acta Biomaterialia - 2008)

[6] Tissue designing:

Viruses have been used to direct cell growth, alignment, and differentiation in biocompatible tissue engineering scaffolds. The surrounding environment has an impact on cell behavior, both in biological cues like the existence physical signals including topology and mechanical moduli, as well as chemicals, ligands. (Cao et al. - ACS Applied Materials & Interfaces - 2015) Scaffolds can be constructed to govern cells in a way that is suited for applications in control cell division, alignment, and growth using this information. The initial step was to look at cell adherence to viral scaffolds. The adhesion and proliferation of NIH-3T3 fibroblasts were examined using layer-by-layer (LbL) assembly of CPMV and the polymer-poly (diallyl dimethylammonium chloride) (PDDA), with higher layer counts indicating greater CPMV adsorption and proliferation. (Gleba et al. - Current Topics in Microbiology and Immunology - 2013)

[7] Agricultural applications:

The implementation of plant viruses in agriculture is an intriguing area that has only recently been considered. A groundbreaking study used abamectin-loaded RCNMV to battle parasitic root nematode infections. (58) It was observed that these particles have greater movement in the soil, boosting the bioavailability of abamectin. The neutrally charged insecticide can be injected into RCNMV using ligand gating for infusion. The abamectin payload is shielded from oxidation and can be delivered gradually. (Wen & Steinmetz - Chemical Society Reviews - 2016)

[8] Plant-based pharmaceutical production:

The fast synthesis of a protein essential to pharmaceutics using an expression vector based on TMV was demonstrated in one of the initial examples of infecting plants with viral vectors. By inserting the gene into a TMV plasmid, researchers were able to produce a high-level heterologous production of physiologically active -tricho santhin, which can prevent HIV replication in vitro. (Hefferon - Application of Plant Viruses in Biotechnology - 2021)

VII. DRAWBACKS

1) Despite cheap operating costs for plant construction, industrial-scale articulation has large upfront costs.
2) In cycles of substitution of hereditary material in plant infection, downsides like immunogenicity, cytotoxicity, fiery response towards viral vectors, and insertional mutagenesis of quality conveying viral vectors prompt the upsurge of non-viral vectors for upgraded quality treatment.
3) The client's expectations of what a drug can do can impact the medication's effect. Doubts about therapeutic effectiveness, side effects/adverse effects of medications, etc. toxic consequences, reactions to Allergens may influence the overall effect. (Khandel et al. - Journal of Nanostructure in Chemistry - 2018)

VIII. CONCLUSION

Generally speaking, infections have been taken advantage of by the improvement of a bewildering exhibit uses that comes under the expansive extent of medication, biotechnology, and energy. While certain regions in medication, like immunizations and quality conveyance, have been around for some time, the utilization of infections in different regions, for example, drug conveyance and tissue designing, have as of late been conceptualized and created. The field of infection-based devices for detecting, evaluating, catalyzing, culturing, and medication development has seen significant advances in biotechnology, but there is much to be done to improve the viability of some diseases' diagnosis and treatment.

A few achievements are the widespread usage of phage display, the commercialization of armored RNA as a molecular screening control, and the efficient and affordable nature of scaled-up pharmaceutical manufacturing in plants. Recent intriguing developments include the efficient catalysis of hydrogen for the creation of clean fuel and the use of plant viruses to combat plant illness.

IX. ACKNOWLEDGMENT

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