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A REVIEW ON THE PLANT MEDIATED SYNTHESIS OF ZINC OXIDE NANOPARTICLES

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Abstract: Metal oxide nanoparticles — zinc oxide, copper oxide, tin oxide, aluminum oxide, etc. have received a lot of attention lately. This is a result of the wide variety of innovative uses in various industries. Because of its incredibly excellent antibacterial, antiviral, and antidiabetic capabilities, zinc oxide nanoparticles (ZnO Nps) have a vital role in restorative applications. ZnO has a white appearance and is water insoluble. They do not affect human cells, but they do harm bacterial cells. Because smaller-sized nanoparticles have greater antibacterial activity, it is crucial to manufacture them. However, the synthesis process should be straightforward, inexpensive, and repeatable. Numerous techniques for synthesizing ZnO Nps have been investigated during the past few decades. The purpose of this work is to explore green synthesis techniques for ZnO Nps utilizing plant extracts. Because they use less harmful chemicals, are environmentally benign, and allow for the one-step synthesis of nanoparticles, researchers are using green synthesis techniques at a rapid rate. Microorganisms such as bacteria, fungus, algae, and yeast, as well as plants and their derivatives, are the biological systems engaged in the environmentally friendly synthesis of nanoparticles. Since ZnO Nps are thought to be harmless, nontoxic, and biocompatible, they are of great interest. Because the size and morphology of ZnO Nps determine their uses in different domains, it is critical to synthesize ZnO Nps with the appropriate size and shape. The green synthesis of ZnO Nps primarily uses a variety of plant extracts. This is as a result of the biomolecules included in plant extracts, which serve as reducing, stabilizing, and capping agents during synthesis. Obtaining plant extracts is as simple as combining the extract with a solvent, such as distilled water. Various plant parts, including leaves, roots, seeds, fruits, flowers, stems, bark, and gum have been utilized. To our knowledge, the green nanotechnology for the synthesis of ZnO Nps is not yet well documented. In the present work, the main objective was to investigate the use of part of plant used for green synthesis, study of different reaction parameters used for the synthesis. Also the biomedical applications of zinc oxide nanoparticles like antibacterial, antifungal, antiviral, anticancer, antidiabetic and drug delivery are discussed. Overall, this study stands as an initial prerequisite step to green nanotechnology research in zinc oxide nanoparticles.

Index Terms **-** Green synthesis, zinc oxide nanoparticles, nanotechnology, metal oxide nanoparticles, plant extracts, antibacterial, antifungal, antiviral, biomedical application

I. INTRODUCTION

Through long-term preventative measures, green chemistry aims to eradicate environmental contamination and reduce the harmful impacts of chemicals on human health. Green chemistry looks for more eco-friendly, alternative reaction medium. Additionally, it looks on methods of lowering reaction temperatures and raising reaction rates. The twelve green chemistry principles were developed in 1998. The book "Green Chemistry: Theory and Practice" by Paul Anastas and John Warner serves as the foundation for the ideas. The government, scientists, and manufacturers are urged in the book to focus their efforts on reducing or eliminating the use of hazardous materials and chemical processes. First principle is Prevention. Preventing waste is preferable. Second principle is atom economy which states that synthetic processes ought to be created in a way that optimizes the final product’s integration of all input components. The third principle is whenever possible, synthetic processes should be created using materials that are either minimally or completely non-toxic to the environment and human health. According to fourth principle products made of chemicals ought to be made as safe as possible without sacrificing any of their intended functions. As per the fifth principle whenever feasible, auxiliary substances should not be used. The sixth principle is about creating Safer Chemicals that is chemical products should be made with as little toxicity as possible while still accomplishing their intended purpose. Seventh principle is about safer auxiliaries and solvent which states whenever feasible, auxiliary substances should not be used. As per eighth principle whenever it is both technically and financially feasible, a feedstock or raw material should be renewable rather than depleting. Ninth principle is about “Reduce Derivatives”. If at all feasible, avoid or eliminate unnecessary derivatization, which includes the use of blocking groups, protection/deprotection, and temporary modifications to physical or chemical processes. This is because these steps might result in waste and need extra reagents. Tenth principle is Catalysis that is selective catalytic reagents are preferable than stoichiometric reagents. Eleventh principle is chemical goods ought to be made in such a way that, upon reaching the end of their useful life, they decompose into harmless byproducts and disappear from the environment To enable real-time, in-process monitoring and control before the creation of hazardous compounds, analytical approaches must be further improved. Last principle is about inherently safer chemistry for Accident Prevention. According to this principle when selecting substances for use in chemical processes, care should be taken to reduce the risk of leaks, explosions, and fires.

II. SYNTHESIS

2.1 Synthesis of NPs from Biogenic Wastes

For prevention of potential health hazards effective solid waste management is essential. Mismanagement of industrial and domestic wastes can cause significant risks to the environment. But, when properly processed and repurposed, biowaste can offer sustainable solutions and reduce its adverse effects. Notably, wastes from plants and animals are biodegradable. Approximately 80% of total biomass stems from post-harvest agricultural waste. This garbage is frequently burned, which results in large emissions of pollution, greenhouse gases, and other pollutants. Common kitchen waste, such as peels from fruits and vegetables, is biodegradable and can be broken down by bacteria and other decomposers. However, when biodegradable waste accumulates in vast quantities, it poses environmental risks. Such garbage can encourage the proliferation of microorganisms, some of which have the ability to infect humans, animals, and plants with infectious diseases. Moreover, waste from the food industry, particularly fruit waste, and agricultural crop residues are abundant and typically require no pre-treatment. This accessibility positions biodegradable wastes as potential raw materials for green synthesis of metal and metal oxide nanoparticles. Leveraging these wastes for nanoparticles synthesis not only mitigates environmental pollution but also supports waste reduction, reuse, and economic enhancement by decreasing high-energy waste accumulation.

Nearly all agro-industrial byproducts and food residues contain phenolic compounds with functional groups that facilitate reduction and ensure stability. Flavonoids, present in fruit-derived biomass waste, can chelate and transform metal ions into NPs. This property underlines their application in NP synthesis [1].

2.2 Synthesis using plant extracts

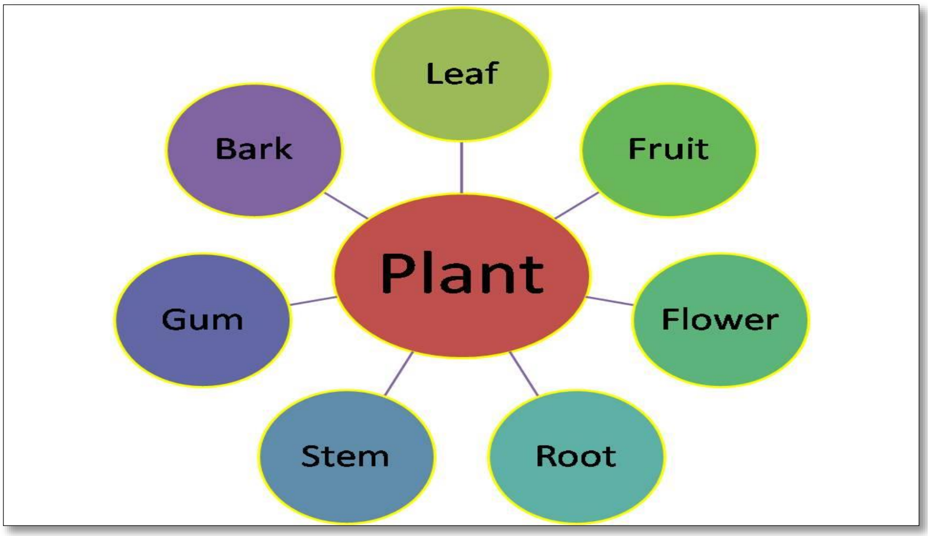

Fig. 1: Synthesis of zinc oxide nanoparticles using different parts of plant.

Plants belong to unique taxonomic group like Lamiaceae, Fabaceae, Rutaceae, Euphorbiaceae and others. There are around 452 plant groups, and each individual plant being source of phytochemicals. Plants in desert-like environment store exclusive kinds of phytochemicals. Plant parts such as roots, stems, leaves, and seeds have been utilized to create NPs. The content of plant extracts plays a crucial role in the production of NPs and is in charge of their bioreduction. Extracts of plants consist of metabolites that decrease bulk metal salts to nano-sized particles. NPs produced are very pure and of enhanced quantity that is free from contaminations PEs can be used in either fresh or dried form. Due to water content, dried plant parts are preferred. While the fresh plant parts are chopped into fragments, the dried plant parts are ground. Plant parts are dried in the sun or in the shade. Owing to the time-consuming nature of this method, oven drying has gained popularity. The extract of different plant leaves is mixed with the precursor (MIs) solutions under different reaction conditions to create NPs aided by the extract. Plant leaf extract requirements, which include phytochemical kinds, concentrations, metal salt concentrations, temperature, and pH, are known to affect the rate, yield, and stability of nanoparticle formation [2]. Plants contain compounds such as flavonoids, phenols, alcoholic sugars, terpenes, alkaloids and reductase which act as reducing agents. It is recognized that medicinal plants are rich in phenols, flavonoids and carbohydrates which have antioxidant potential. Zinc ions are reduced by the antioxidants present in the plant to metallic zinc. The metallic zinc formed reacts with the dissolved oxygen present in the solution to form ZnO NPs. The antioxidants from the plant extracts act as stabilizing agents preventing agglomeration of particles and crystal growth.

Annu et al [3] synthesized using aloe vera plant extract. The main constituents of Aloe vera include hemicellulose, pectin, and lignin which can be the main reducing agents. Gnanasangeetha et al [4] used corriandrum sativum for the green synthesis. For Coriandrum sativum identification of active phytochemicals was done. The phytochemicals which are present are alkaloids, carbohydrates, glycosides, steroid, fixed oils, tannins, protein, flavenoids and terpenoids. Regardless of repeated washing the surveillance proves the subsistence of aldehydes, amines, terpenoids, phenolic compounds were bounded to the surface of ZnO nanoparticles. It enhances stabilization. The physicochemical properties of corriandrum sativum acts as a biotemplate which prevents the particles formed from aggregating. Bala et al [5] also conducted phytochemical analysis of plant extract and determined the total phenolic content, total flavonoid content, reducing sugar content and starch content in leaf extract of Hibiscus subdariffa. Phytochemical analysis of plant extracts revealed that phenolics, flavonoids, ascorbic acid, reducing sugar and starch present in the plant extract can trigger reduction of salt and even control the size of nanoparticles. Free amino and carboxylic groups of proteins, alkaloids, phenolic or flavonoids, present in the plant extract may bind to the surface of zinc and trigger the formation of ZnO NPs. Amides from C=O, C=O-C and C=C groups of heterocyclic compound may act like a stabilizer.

Table 1: Green synthesis of zinc oxide NPs using leaves of different plants

Part of plant	Salt precursor	Particle size	Morphology	Application	Ref no.
Plant extract(which part of plant is used not mentioned) *vulgaris, cinnamomum tamala, cinnamomum verum, brassica oleracea*	Zinc nitrate	20 30 46 47	Spherical Rod Rod Spherical	Antimicrobial	6
Rubia tinctorum	Zinc acetate	40 nm	Spherical	Breast Cancer treatment	7
Ulva Lactuca seaweed	-	10-50 nm	-	Photocatalytic, antibiofilm and insecticidal	8
Ferulago angulata schlecht boiss extract	Zinc acetate	44 nm	-	Photocatalytic activity	9
Tillandsia recurvata	-	12-61 nm	Flake like structure	Photocatalytic activity	10
Aloe vera					3
Leaf extract					
corriandrum sativum	Zinc acetate	66nm 81 nm	-	-	11
Laurus nobilis	Zinc acetate and zinc nitrate	21.49 and 25.26 nm	-	-	4
paceiflora	Zinc acetate		Antibacterial		12
Hibiscus subdariffa	Zinc acetate	30 nm	Spherical, cauliflower, dumbbell	Anti-bacterial	13
Hot and cold aloe vera leaf extract	Zinc nitrate	100nm	Rod Rod Sphere	*Antibacterial property*	14
Camellia sinensis leaves,	Zinc acetate	18 nm		*Antibacterial and antifungal*	15
Eucalyptus globules		11.6 nm	Spherical	Photocatalytic	16
Limonia acidissima	Zinc nitrate	12 to 53 nm	Spherical	*Tuberculosis treatment*	17
Agathosma betulina	-	15.8 nm	Spherical	Nonlinear VI characteristic for Variastor response	18
Calotropis Gigantea	Zinc nitrate	30-35 nm			19
Solanum nigrum	-	29.39 nm	Quasispherical	Antibacterial activity	20
1Calotropis procera	-	15-25nm	Spherical	Photocatalytic	21

Ocimum Tenuiflorum	-	13.86 nm	-	-	22
Syzygium cumini	-	-	-	Photocatalytic	23
Psidium guajava	-	-	Trigonal	-	24
Tecoma castanifolia	-	70-75 nm,	spherical	Antioxidant, antibacterial, anticancer	25
Cassia fistula		5-15 nm		Photocatalytic, antioxidant antibacterial	26
Carica papaya		50nm	Spherical	Photocatalytic, photovoltaic	27
Parthenium hysterophorus	*Zinc nitrate*	10nm	Spherical	Antibacterial Seed germination and vegetative growth	28
Olive europaea	*Zinc nitrate*	41nm	Spherical		29
Adulsa and Lemongrass	*Zinc nitrate*	50nm-95 nm	irregular	Catalytic application	30
Chironji (Buchanania lanzan)	*Zinc nitrate*			Photocatalytic, photodegradative, antimicrobial, antioxidant	31
Veronica multifida	Zinc acetate			Antimicrobial, antibiofilm	32
Abutilon indicum, Clerodendrum infortunatum, Clerodendrum inerme		16-20 nm	Sphere and rod	Photocatalytic activities, antimicrobial, antifungal, antioxidant	33
Euphorbia hirta				*Antimicrobial*	34
Allium ursinum z	Zinc nitrate	20-60 nm	Semispherical	Antimicrobial	35
Dittrichia graveolens as reducing agent and turmeric as stabilizing agent	Zinc nitrate			Photocatalytic	36
Coriandrum sativam	*Zinc acetate*	*9-18 nm*	*Hexagonal*	*Photocatalytic*	37
Ocimum basilicum L. var. purpurascens Benth-LAMIACEAE,	Zinc nitrate	50 nm			38

Mostly in the synthesis of nanoparticles the part of the plant which is used most is the leaf. Also out of the different precursors of zinc salt like zinc chloride, zinc nitrate, zinc acetate and zinc sulphate the preferred salt precursors are zinc nitrate and zinc acetate. The other parts of plants which are used are given in table below like fruits, flowers, roots, seeds, bark and gum. In fruit extract fruit juice, pulp, fruit peel or fruit seed is used.

Table 2: Synthesis of ZnO NPs using fruit, flower, root, seed, bark, stem and gum

Synthesis of ZnO NPs					
Fruit extract	**Salt precursor**	**Size**	**Morphology**	**Application**	**Ref no.**
citrus aurantifolia	Zinc acetate	-	Spherical	-	39
tomato, orange, grapefruit and lemon peel extract	Zinc nitrate	-	-	Photocatalytic	40
Citrus sinensis peel extract (oranges)	Zinc nitrate	-	Hexagonal prisms with rounded down corners, oval spheres, sponge like shapes	Photocatalytic	41
Orange fruit peel extract,	Zinc nitrate	10-230 nm	-	Antibacterial	42
Lemon juice	Zinc acetate	21.5 nm	Spherical	Photocatalytic	43
Indian Bael(*Aegle marmelos*) fruit pulp	-	17 nm	sheet and spindle	Photocatalytic, antioxidant, antibacterial	44
Averrhoe carrambola	-	-	-	Photocatalytic	45
Flower extract					
aqueous flower extract of Nyctanthes arbor-tristis	Zinc acetate	-	-	Antifungal	46
Prosopsis farcta	-	16 to 26 nm	-	Antimicrobial application for wound healing bandage application	47
Broccoli	-	14 nm	-	Photocatalytic	48
Seed extract					
Cuminum cyminum (cumin)	Zinc nitrate	18 to 23 nm	Mostly spherical and oval	Antimicrobial	49
Loquat(*Eriobutria japonica* seed extract	Zinc acetate	50 nm	-	Photocatalytic	50
Root extract					
Scutellaria Baicalensis	Zinc nitrate	50nm	Sphere	Photocatalytic degradation of metheylene blue	51
Bark extract					
Cinnamomum verum bark extract	-	45 nm	-	Antibacterial activity	52
Gum					

Prunus dulcis (Almond gum)	Zinc nitrate	30 nm	-	Antimicrobial , supercapacitor applications	53
Stem extract					
Phyllanthus embilica	*Zinc acetate*	25 nm-35 nm	Spherical	Antibacterial activity	54
Saraca asoca	-	-	-	Antibacterial and antibiofilm	55
Calligonum comosum	-	50-100 nm	-	Water treatment	56
Ficus religiosa	-	-	-	Water treatment	57

III. FACTORS AFFECTING SIZE AND SHAPE OF NANOPARTICLES

Morphology of nanoparticles depends upon various factors like reaction temperature, reaction time, salt precursor used, base concentration or pH, rate of stirring [58, 59]. In green synthesis, the morphology of nanoparticles depends on other factors as well such as the type of species of plant used, the type and concentration of biomolecules present in it. Change in any one of these parameters can alter the size, shape and, rate of synthesis of NPs, as well as their morphology and yield. However most of the work is done on the study of effect of temperature and base concentration.

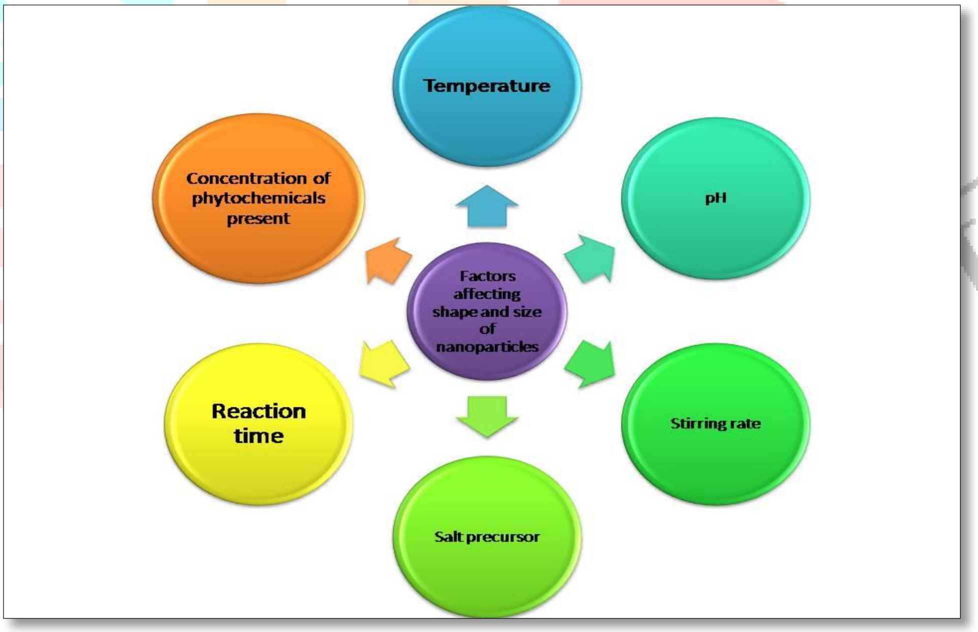

Fig. 2: Factors affecting shape and size of nanoparticles

3.1 Effect of temperature

Particle size and morphology of nanoparticles is very important as properties exhibited by nanoparticles depend on its size and shape. Researchers are working on knowing which reaction parameters are responsible for change in size and shape and they are trying to synthesize nanoparticles of required shape and size. Few papers have reported increase in particle size with increase in calcinations temperature .Very less research is done on reaction temperature involved in wet chemical synthesis. Xiao fang et. al [60] have prepared a series of ZnO nanoparticles with diameter from 17 nm to 110 nm wherein the particle sizes were determined by furnace temperature. The higher the temperature, the larger the particle size was obtained. F. Li et al [61] reported change in shape from nanodisk into rings with increase in temperature. C.C. Lin et al [62] reported increase in the thickness of nanowires synthesized when the growth temperature increased from 70^0C to 95^0C. According to Ruby Chouhan et al. [63], as the temperature of calcinations is raised from 300^0C to 1000^0C, the diffraction peaks sharpen and grow stronger, indicating an improvement in the crystal quality of the nanoparticles and an increase in their sizes. Nevertheless, it appears from Chung-Hsin Lu et al. [64] that increasing the reaction temperature somewhat lowers the ZnO powder manufacturing yield and particle size. In this case the ZnO nanoparticles are synthesized by hydrothermal method. For the formation of one-dimensional nanostructure anisotropic growth of material is required. That means the crystal should grow along a certain orientation faster than the other directions. According to Ravi Chand Singh et al [65], the driving force for the synthesis of nanorods is the decrease in Gibbs free energy because of low supersaturation. Eventually at room temperature at proper synthesis conditions, synthesis of zinc oxide nanorods takes place. At an elevated temperature due to high supersaturation there is no reduction in Gibbs free energy, which results in homogeneous nucleation leading to isotropic growth of zinc oxide powder, and one gets isotropically grown particles instead of rods. Here they reported that diameter of nanorods grows with increase in the sintering temperature. The sintering temperature promotes enlargement of grain boundaries and consequently particle size increases. Urai Seetavan et al [66] reported increase in size of the nanoparticles when the calcinations temperature is increased from 400^0C to 650^0C. Preetam Singh et al [67] reported a linear increase in lattice parameters with temperature along with increase in the size of the grains. As the temperature increases from 100^0C to 700^0C particle size changes from 15.2 nm to 21.8 nm. P. M. Aneesh et al [68] also reported increase in particle size with increase in reaction temperature. Ozlem Yildirim et al [69] however reported that the particle size is greatly affected by the precipitation temperature. Higher precipitation temperature leads to an increase in the nucleation events and it leads to smaller ZnO precipitates.

3.2 Effect of base concentration

Radyum Ikono et al [70] have studied the effect of pH on particle size on the zinc oxide nanoparticles. They have synthesized nanoparticles using sol gel method. The particle size increases with change in particle size and also the purity. In this paper they have studied the effect of pH on the purity of the synthesized samples as well. At low pH the additional peak corresponding to zinc hydroxide is obtained which vanishes at higher pH value. Jianfeng Jin et al [71] also synthesized the zinc oxide nanoparticles using sol gel technology to study the effect of pH on morphology. According to their study with pH the morphology and the particle size changes and they found that as the pH increases particle size decreases. So there is a discrepancy between the results stated by above two researchers. They justified the behavior stating that the pH value influences the sol hydrolysis and condensation behavior. In addition it controls the value of H^+ and OH in the solution and hence determines the metal oxygen bond formation. The activity of Zn^+ decreases in alkaline media. Swaroop et al [72] have also studied size variation and morphology variation in ZnO nanoparticles. They synthesized the nanoparticles using co precipitation method. They obtained significant change in morphology and lattice strain with change in pH value for low pH they got hexagonal structure while at higher pH they obtained plate like structure. In all the three papers mentioned above the salt precursor used is zinc acetate. In this paper they observed with increase in pH the particle size decreases. Rizwan Wahab et al [73] also studied the same thing in precipitation synthesis of zinc oxide nanoparticles using zinc nitrate as the precursor. A systematic variation from sheets to micro flowers is obtained as the pH value changes from 6 to 12. The amount of H^+ and OH^- are found a key to control the structure of material. Possible growth mechanism with change in pH is mentioned in this paper. S. Shankar et al [74] spin coated ZnO thin films at differ rent pH values. They studied the influence of pH on the thickness of the film and they found that as the pH increases the thickness of the film decreases. Sahebali et al [75] synthesized ZnO nanostructures using Gelatin method. They observed that when pH is lower than 7 grain size is almost constant, which means acid solution could restrain grain growth. When pH value is higher than 7 its total alkali environment enhances grain growth. In this paper they tried to control hydrolysis. It is known that acid usually restrain hydrolysis while alkali accelerates the hydrolysis. When pH is higher than 7 which means environment do benefit to accelerate hydrolysis, the huge aggregated particles are formed and grain tend to grow quickly. H.A. Rafaie et al [76] studied the effect of pH on the growth of nanorods. Growth inhibition was observed in the sample synthesized at pH 5 which can be due to preferential erosion of ZnO (0001) face. Enhanced growth in alkaline solution at pH 9 was due to the more abundance OH compared to acidic solution which promoted the intermediate molecule $Zn(OH)_2$. Equally efficient growth at pH 7 indicated that erosion process dominated the inhibition of nonorod growth over enhancement due to the presence of OH^- . Alias et al [77] studied effect of pH on ZnO nanoparticles. They reported that the OHions allow the nucleation and growth of ZnO and the formation of particles. Particle size decreases when the pH of the sols is above 9 because the amount of dissolved OH^- was larger during synthesis of ZnO at pH > 9. When ZnO reacts with too much OH^- the dissolution of ZnO occurs. The crystallites and particles shrank and clumped together as a result of the disintegration. Noel Nesakumar et al

[78] reported change in structural morphology from nanospheres to nanorods on varying pH from 11-10.7. M. Jay Chithra et al [79] reported that the intensity of the peaks changes as the pH changes.

In controlling shape and size of Nps, pH plays an important role as pH and temperature also controlling nucleation formation. Reaction pH variations may affect the produced NPs' shape and size. The acidified media, on the other hand, form a range of diverse sized particles when compared to lower acidic pH. The size and form of ZnO NPs created may modified in the reaction pH. In chemical synthesis also alkaline environment produce smaller sized spherical nanoparticles [58, 59]. In green synthesis alkaline pH environment favours phytochemical deprotonation and activation. Lower pH leads to decreased reduction or capping activity of metal salts. Overall, Nps created in an alkaline reaction mixture are found to be more stable as compared to NPs created at acidic pH. Temperature is another important factor to consider in any synthesis. Temperature is a critical factor that changes the size and shape of NPs. In green synthesis increase in temperature shows catalytic behavior and found to increase the rate of reaction. Chemical synthesis of ZnO Nps normally requires the temperature of the order of 60^0C-80^0C while for green synthesis temperatures of about 100^0C are needed. Concentration of reducing agent increases particle growth. Extremely concentrated biological extracts lead to bigger sized Nps. Precipitation method consists of four stages of synthesis i.e. precursor formation, nucleation, growth, and aging.

Before nucleation can occur, zero-charge precursor molecules need to be formed. The group of precursor molecules results in a supersaturation. Further growth from the supersaturated solution takes place. After nucleation and growth, the average particle size may change because of aging.

After nucleation and growth, nanoparticles have been formed with a specific size distribution. The nucleation rate increases strongly with decreasing surface energy and increasing supersaturation. The supersaturation increases with decreasing solubility of the metal oxide, and thus, the metal oxide properties have a strong influence on the nucleation rate.

IV. ROLE OF CONCENTRATION OF PLANT EXTRACT

Concentration of plant extract plays a vital role in the synthesis of ZnO Nps. Insufficient amount of bioactive compound lowers the yield of ZnO whereas sufficient amount increases the yield. That means it will reduce all Zn^{+2} ions present in the reaction mixture. Senthilkumar et al[10] reported that the higher percentage of phenolic compounds with antioxidant potential provide the reducing action on the metal oxides and significantly present amino acids, protein and lipis helped to stabilize the growth of nanoparticles. Fresh tea leaf is rich in flavonol group of polyphenols. These polyphenols are known as catechins (approximately) 30% of the dry leaf weight. Other polyphenols present are flavonois and their glycosides, chlorogenic acid, gallic acid, coumarylquine acid and theogallin. Green tea is usually prepared without fermentation and hence the composition of green tea is very similar to that of fresh leaf. Composition of green tea leaf is phenolic compounds (30%), proteins (15%), amino acids (4%), carbohydrates (7%), lipids (7%), vitamins C and E. Phenolic compounds are good antioxidants. We know that antioxidants are good reducers of metal ions. Hence it favors green synthesis. Higher contents of proteins, lipids and amino acids help to stabilize the growth of nanoparticles and inihibit agglomeration.

Raut et al [22] used tulsi leaves for the green synthesis. Chemical constituents of tulsi are linalool, alkaloids, ursolic acid, glycosides, carvacroll, tannins, rosmarinc acid, aromatic compounds etc.

V. PHYTOCHEMICAL ANALYSIS

The table below shows the different tests done to find out the kind of phytochemicals present in the plant.

Table 3: Different tests for identification of phytochemicals

Name of the compound	**Name of the tes**	**Result**
Flavonoids	Shinoda test	Appearance of red colour indicates the presence of flavon
Alkaloids	Mayer test	A creamish precipitate revealed the presence of alkaloids
Phenolic compounds	Ferric chloride test	Deep green colour
glycosides	Borntrager test	Pink colour

Steroids	Salkowski Test	reddish brown colour
Proteins were evaluated by	Millon test	White precipitate
Terpenoid		Green colour

D. Suresh et al [26] carried out the flavonoid assay using Swainand Hillis method. The flavonoid content in the plant extract was measured with reference to the standard Gallic acid values. Agarwal et al [55] synthesized ZnO NPS using saraca asoca leaf extract. and the antibacterial and antibiofilm activity of green synthesized ZnONPs was measured against the biofilm-producing bacteria Bacillus subtilis. The ZnO NPs were found to have a concentration-dependent effect on the biofilm biomass of the preformed or matured biofilms, with values of 68%, 50%, and 33% at 0.5 × MIC, 0.75 × MIC, and 1 × MIC. Additionally, the results of flow cytometry point to bacterial cell membrane degradation. Comparing the NP concentration to the control, the data showed that the percentage of dead cells rose. Therefore, it can be concluded that the green synthetic ZnO nanoparticles showed excellent antibacterial and antibiofilm activity against the Bacillus subtilis bacteria that produce bio-films and that they could be a promising substitute agent for the treatment of biofilms and drug-resistant bacteria.

Gharbi et al [56] synthesized using extracts from Calligonum comosum L. leaves. Evaluating the generated catalyst's photocatalytic effectiveness against organic pollutants is the main goal of the study. Average particle diameter is about 50–100 nm while crystallite size is found to be of the order of 62.3 nm, respectively. Band gap energy is determined to be 2.3 eV.

Pandey et al [57] synthesized using leaves of Ficus religiosa. The Ficus religiosa tree, also known as the peepal tree in India, Pakistan, and Bangladesh, is holy. In the traditional system, leaves, roots, fruit, and bark of peepal tree were used in pharmaceuticals. The leaves of Ficus religiosa contain several phytochemicals such as myricetin, kaempeferol, vitamin-K, n-octacosanol, and quercetin, which act as stabilizing as well as a reducing agent that can be used to cap and protect metal oxide nanoparticles during their synthesis. These metal oxide nanoparticles can be used efficiently for the removal of toxic effluents from synthetic and real water samples via various approaches such as adsorption, membrane filtration, photocatalysis, etc. Studies by Bala et al [13] suggest that the crystallinity of sample increased with increase in temperature.The samples which are synthesized at low temperature (60) FTIR spectrum shows phytochemical compounds were absorbed on the surface of ZnO. However when the sample is synthesized at (100), the FTIR spectrum shows that either those phytochemicals are either absent or remained absorbed on ZnO nanoparticles in small amount. These differences were because of rise in temperature. Because of calcinations at high temperature bioactive compounds are lost.

VI. BIOMEDICAL APPLICATIONS OF ZINC OXIDE NANOPARTICLES

Antibacterial properties are displayed by zinc oxide nanoparticles. Their nature is oligodynamic. They exhibit toxicity to prokaryotic and eukaryotic cells as well as viruses, fungus, algae, and bacteria. Antibacterial agents find widespread application in the food packaging, water purification, textile, and pharmaceutical industries. It has been discovered that organic chemicals are harmful to human health. As a result, inorganic disinfectants such metal oxide nanoparticles are being used more often. Zinc oxide nanoparticles kill bacteria on the spot without endangering the tissues around them. Numerous studies have looked into zinc oxide nanoparticles' antifungal properties. To quote, research on the antifungal properties of zinc oxide nanoparticles against candida albicans has been conducted by Sinouvassane Djearamane et al. [80]. There was also discussion of the mechanism underlying ZnO Nps' antifungal properties.

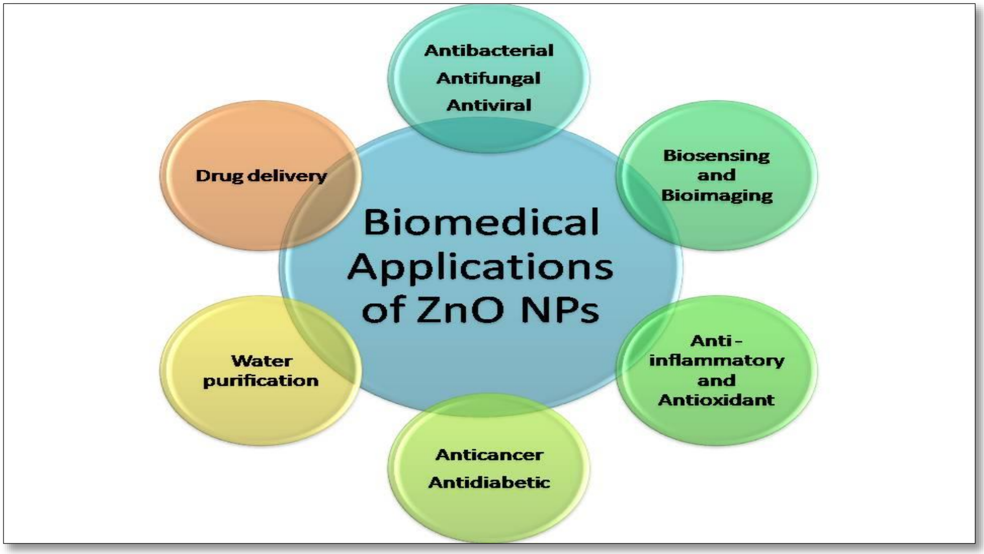

Fig. 3: Biomedical applications of Zinc oxide nanoparticles

VII. MECHANISM OF ANTIFUNGAL PROPERTY OF ZINC OXIDE NANOPARTICLES

There is ongoing discussion over the antibacterial mechanism of metallic nanoparticles. The main theories, according to scientific reports, are that the interaction between NPs and the cell membrane inhibits the synthesis of cell walls, enzyme activity, and cell signaling; additionally, DNA damage, ribosome disassembly, inactivation of protein synthesis, and structural modifications of essential proteins result in the formation of reactive oxidative species (ROS) and the release of metal ions from the NPs. Apart from the membrane malfunction resulting from the concentration of positively charged Zn^{2+} due to ZnO NPs dissolving on the cell membrane, ZnO NP internalization impairs microbial metabolic activity and ultimately leads to microbial cell death. The antiviral capabilities of ZnO nanoparticles have been thoroughly reviewed by Mahda S. Nasrollahzadeh et al. [81]. The findings demonstrated that zinc oxide nanoparticles (ZnO NPs) had unique physicochemical characteristics that make them a potentially effective strategy for creating nanovaccines and antiviral drugs, particularly against RNA viruses like the human immunodeficiency virus (HIV) and severe acute respiratory syndrome coronavirus. The most likely antiviral mechanistic mechanisms for ZnO NPs involve deactivating the virus through virostatic potential and preventing the virus from entering the cells. Zinc has been demonstrated in the past to have antiviral properties against a wide range of viruses, such as severe acute respiratory syndrome coronavirus, hepatitis E virus (HEV), hepatitis C virus (HCV), rotavirus, rhinovirus, picornavirus, HSV, and human immunodeficiency virus (HIV). Research on the formation of ZnO NPs for the prevention and treatment of viral infection has received a lot of attention recently since zinc-containing therapies have been demonstrated to enhance immune response. The effectiveness of ZnO NPs against viral infection is reviewed in the current study. Zinc has been demonstrated to operate through a number of pathways, including the host's immune response modulation. This is because zinc strengthens the defense mechanisms mediated by natural killer (NK) cells against infections, which allows ROS to bind with and destroy the virus envelope. Based on the previously given information and the proposed mode of action, zinc oxide nanoparticles (ZnO NPs) are anticipated to target many RNA viruses, such as HIV and coronavirus infection. This assertion is primarily supported by ZnO NPs' virostatic, electrostatic, and other physiochemical characteristics, including their size, shape-modifiable nature, and surface characteristics. However, this idea cannot be confirmed without additional analysis. Zinc salts may be helpful in strengthening immune responses against viral infection, but their use may be restricted due to potential imbalances in zinc homeostasis in serum and plasma, which may raise the risk of aging, Alzheimer's disease (AD), and other neurodegenerative disorders. Recently, a great deal of research has been done to advance the technology of nanofluids, which can enhance their hydrodynamic qualities and stability and make using nanomaterials as medications simpler and safer. Consequently, it is advised that a thorough investigation be conducted on humans in order to assess these advantages and potential hazards [82]. Studies on the use of ZnO NPs in medication delivery have been conducted by Abhishek Nigam et al. [86]. The chitosan polymer has enveloped the ZnO nanoparticles. ZnO nanoparticles' drug loading and drug release capabilities have demonstrated a stronger influence on drug delivery. Anticancer: Due to their selective cytotoxicity against cancer cells, zinc oxide nanoparticles have been proven to be effective in the treatment of cancer. Zinc oxide nanoparticles with a size of less than 20 nm and a high concentration of these particles may have an impact on healthy human cells. However, engineering design can be used to increase the cell selectivity of these nanoparticles while reducing harm to healthy cells. One of the distinctive properties of zinc oxide nanoparticles' cytotoxicity towards cancer cells has been shown to be their capacity to cause oxidative stress in these cells. This characteristic results from ZnO's semiconductor nature. ZnO causes the production of ROS, which causes oxidative stress and ultimately cell death.

VIII. CONCLUSION

The leaf is the most frequently utilized portion of the plant. Fruit extract is the second most desired portion of the plant, according to a literature review conducted after the leaf. Other parts used include root, stem, flower, gum, and other sections in addition to leaf and fruit. Zinc nitrate is the most widely used salt precursor, with zinc acetate coming in second. This review centers on the latest developments in environmentally friendly zinc oxide nanoparticle production. It also discusses the benefits of green synthesis over conventional techniques, emphasizing its affordability, ease of use, and environmental friendliness. In the end, it is hoped that the literature already in existence in this field will be improved and provide insights that will direct researchers in their further work. This review will offer a thorough investigation of this specialized subject.

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