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Advanced Materials in Cancer Therapy

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Abstract

The overview of this review article depends on the various techniques of formation of silver nanoparticles and different application take place in medicinal point of view.

The branch of nanotechnology plays an important role in medical science research. In this different nanoparticle is synthesized which have various application in gene delivery, drug delivery and reduce the toxic effect of drugs in the human body and also act as an antibacterial in pharmaceutical industries.

In recent days silver nanoparticles have had an important role due to their optical and catalytic properties. A large number of different particles or methods are used to prepare the different shapes of silver nanoparticles used in drug delivery. Different shapes of nanoparticles have increased their demand in various researches depend on medicinal uses. Silver nanoparticle preparation can be studied by 3 techniques related to irradiations, chemicals, bacteria, fungi, and plants.

Nanomedicine have a large number of advantages in treating various chronic diseases by using biological agents, chemotherapeutic agents, and used to deliver the drug to a specific site of the body. A silver nanoparticle is prepared for detection tool to detect the adverse effect of diseases on the target cell. Nanoparticles are used in cancer therapy to remove the damaged cell of the body.

INTRODUCTION

In recent years, the tremendous growth of research and application has taken place in the field of nanoscience and nanotechnology. The increased use of nanotechnology in medicine has a notable boost in detection and therapy. Implementation in medicines involves drug administration both inside and outside the body. (Duncan R et al 2005, Ferrari M. 2005,Fattal E et. al 1998).

Before going into details, first of all, let understand the basic idea about first drug delivery and second nanotechnology.

Drug delivery- Drug delivery is a phenomenon or a process in which therapeutic effect is achieved by the administration of the pharmaceutical compound in humans or animals. Nowadays, nasal and pulmonary routes of drug administration are high in use and have become popular and gaining importance for the therapy of human disease. For peptide and protein synthesis, scientists have found favorable substitutes to parenteral drug delivery.

For this purpose, many drug administering systems are formulated and some of them are under investigation for pulmonary and nasal delivery. These include prodrugs, microsphere gels, liposomes, cyclodertrins, proliposomes, etc.

Nanoparticles made up of biodegradable polymers must fulfill the requirements of these drug delivery systems e.g.

- Bioavailability and biocompatibility.
- Can be converted into an aerosol.
- Must be safe against the force of aerosolization.
- Aiming at a distinct site.
- The drug must be released presently.
- Decaying within an admissible time.

Metallic nanoparticles have some antibacterial properties to be utilized in the delivery of drugs and easily forming the route to enter in vessels of the human body and to prevent another effect on the body (Krishna R et al. 1996, Thacharodi D et al. 1996, Bhat M et al.1995, Panchagnula R. 1997). The second is what is nanotechnology- Is defined as the field of research and innovation concerned with building things. Generally, materials and devices are on the scale of atoms and molecules.

Nanotechnology is being utilized in establishing countries in preventing health issues. The umbrella term for this kind of nanotechnology is Nanomedicine. Nanotech is implemented in numerous industrial and purification processes. Not all

atoms/molecules are utilized for clinical processes obey the newly suggested and now conventionally assumed definition of a size <100 nm. (The Royal Society 2004). Nanoparticles are used for clinical purposes because of their vital and interesting property, e.g. their surface to (congeomerate) mass ratio. They have greater than many other substances, their quantum. Features and adsorption and carrying properties (Cascone MG et al. 2002). Nanoparticles have a comparatively greater surface, enabling for binding then adsorbing it hence carrying substances like medicines, probes, and proteid (protein) (Baran ET et al. 2002, Kipp JE 2004).

However, solid Nanoparticles can be employed as medicine targeting, when they reached the infected area in the body they released the drug to the affected site. So nanoparticles must be a biodegradable compound to achieve an effective transport or release of a drug. (Bamrungsap. S et al. 2012).

Nanoparticles are of two types: Organic nanoparticles (Liposomes, Dendrimers) and Inorganic nanoparticles (Metallic nanoparticles, Silica nanoparticles (Safari, J et al. 2017, Sakamotoa J.H et al. 2010).

In this, we will discuss only, metal nanoparticles that are silver nanoparticles. There are mainly two routes for the synthesis of metal nanoparticles. (a)Physical approach and (b) Chemical approach.

The physical approach has the following methods: Laser ablation and evaporation- condensation. The Second is the Chemical approach; this includes precipitation of metal ions in produced conditions promoting the successive formation of small metal clots and precipitates. (Khomutov G et al. 2002, Oliveira M et al. 2005, Egorova, E.M et al. 2000).

Based on the type of reducing agents, the classical chemical method is used by using different types of reducing agents (hydrogen, lithium, aluminum hydride, sodium borohydrides, DMH) and radiation are used to generate solvated electrons and do the reduction process (Pileni 1997, Leff, D.V et al. 1995, Butenko, A.V et al. 1990).

Chemical methods are further divided into two types (a) by using non deleterious solvent and (b) naturally occurring reducing agent or reducing agent obtained naturally e.g. plant extracts such as polysaccharides.

Using microorganisms- bacteria and fungi as reductants and third is reverse micelles system in which phenomenon of accumulation happens in the hydrous core of reverse micelles and molecular of surfactant surrounds the growing particles (Petit, C et al. 1993, Lisiecki, I et al. 1995).

Two main forces that govern the stability of nanoparticles are steric and electrostatic. The electrostatic force is the force of attraction between the opposite species that is anionic species are attracted by cationic species. Anionic species e.g. Halides, polyoxoanion, or carboxylate get attracted towards cationic species i.e. metal particles. When this type of force works leads to the generation of the electrical double layer that results in the generation of coulombic repulsion force between the nanoparticles. The presence of bulky groups like organic materials because of their huge size, hamper nanoparticles from diffusing together, result in steric stabilization. Large bulky groups like polymers and large cations such as alkyl ammonium work as steric stabilizers. The solubility of metallic nanoparticles also depends on the type of stabilizers used. (Templeton, A.C et al. 2003).

Metallic nanoparticles exhibit different shapes, sizes, distribution, and properties which also depend on the method of synthesis done by using reducing and stabilization agents and controlled by chemical agents due to these different properties of metal nanoparticles utilized in many different areas of Nanomedicines. (Yeo, S.Y et al. 2003, Chimentão, R.J et al. 2004, He, B et al. 2004).

Silver has various forms and is being used for various purposes from time immemorial. The study says silver has shown extensive antibacterial property and the same has been store water in a silver container by fumigating portable water. (Amato E et al. 2011).

Fabrication of Silver Nanoparticles

The application of silver nanoparticles is increasing in various fields therefore the formation of the metal nanoparticle is very common. (Parveen et al., 2012) the size and shape of nanoparticles are based on some properties and characteristics such as color, temperature, magnetic behavior due to this property different shapes of the silver nanoparticle are synthesized. The silver nanoparticles have good conductivity and chemical stability and also have special electrical and optical properties. That's it get more attention in recent years in various industries such as medical science, drug delivery food industries, and anti-bacterial properties. By the two methods, the silver nanoparticles of large quantity are formed one is top-down, and another is a bottom-up method (Parveen, S et al. 2012, Gurunathan, S et al. 2009, Ahmad, A et al. 2003,Hill 1939).

The prepared nanoproducts' shape and size can be control by altering the factors such as (stabilizing and reducing) and also the methods of synthesis. (Yeo, S.Y et al. 2003, Chimentão, R.J et al.2004). The different shapes of the silver nanoparticle can be synthesis by a different method.

The fabrication of silver nanoparticles can be done by three approaches:

- Physical approach
- Chemical approach
- Green approach

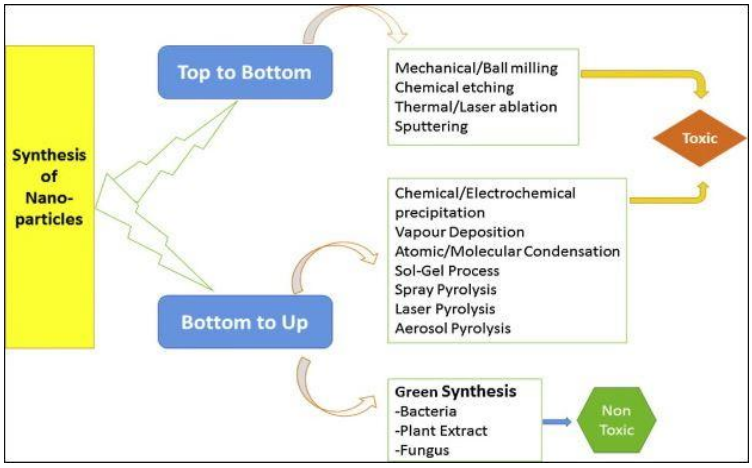

Figure 1: Fabrication of Nanoparticles (Gurunathan, S. et al. 2009)

FABRICATION BY PHYSICAL APPROACH

The physical approach for the synthesis of AgNPs can include evaporation-condensation and laser ablation methods to form more quantity of nanoparticles without using toxic chemicals (Amendola, V et al. 2009, Iravani, S et al. 2014).

The first technique is evaporation-condensation is taken place by using tube-furnace which has a boat-like large space in the center and it can evaporate or vaporize with the help of carrier gas and several uniforms. NPs like Au, Ag, fullerenes can be formed by this technique (Magnusson, M.H et al. 1999, Schmidt-Ott 1998, Gurav, A.S et al.1994). But there are many disadvantages of a tube furnace are it requires a lot of space for the preparation of silver nanoparticles. Due to the large surface, high energy is required so the temperature of the source material heats the surrounding environment. It is time-consuming to attain thermal stability. The source material also consumes high power of several kilowatts to gain stable performing temperature. (Kruis F et al. 2000, Magnusson M.; et al. 1999).

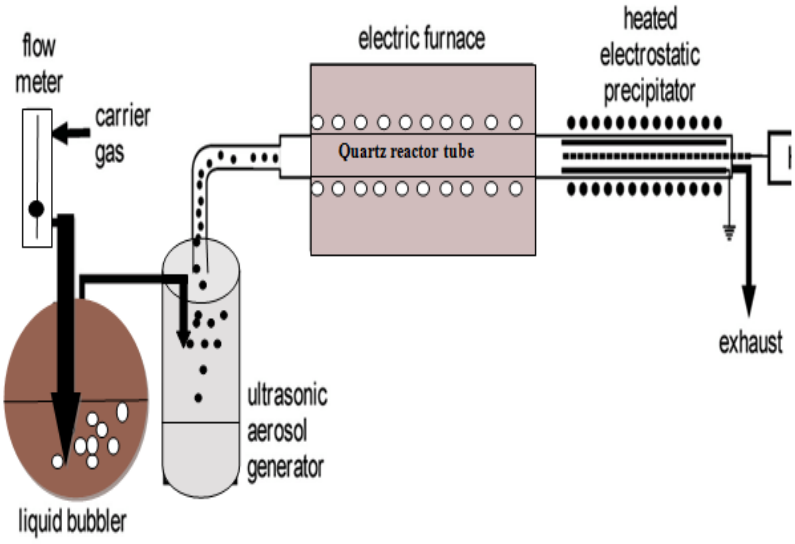

Figure 2: Image of the tube furnace

To prevent from happening this (Jung, J.H et al. 2006). Use a small ceramic heater for the synthesis of AgNPs in high concentration they require the heater to evaporate source material. Then by using a condenser the evaporated vapor can be cooled at a suitable rapid rate. Because the area surrounding the heater surface has a sharp temperature, a gradient in comparison to tube furnace in due to no fluctuation in the temperature the stable nanoparticle is generated.

The small heater consists of applications of inhaling, toxicity, and long-duration experiment and calibration device for prepared silver nanoparticle measurement (Jung, J.H et al. 2006). The prepared AgNPs can have a range from 6.2-21.5 nm and 1.23-1.88 nm is synthesized even in high heater temperature and at a high concentration.

Second another method of physical approach is laser ablation by this method pure metal colloids are synthesized with the help of laser pulses (Femtosecond laser pulses and Nanosecond laser pulses).by using the laser ablation technique on the bulk material of metal in dissolved form, AgNPs can be synthesized (Mafune F. et al.2000, Kabashin AV. et al. 2003, Dolgaev SI et al.2002). The uncontaminated metal colloids formed by this method and it is based on different factors like time duration of laser pulses (in a nanosecond and Femtosecond regime), aqueous medium of synthesis, laser ablation time, present or absence of surface-active agents, laser fluencies, and wavelength of the laser beam on metal object (Kim S. et al. 2005, Tarasenko N et al. 2006).

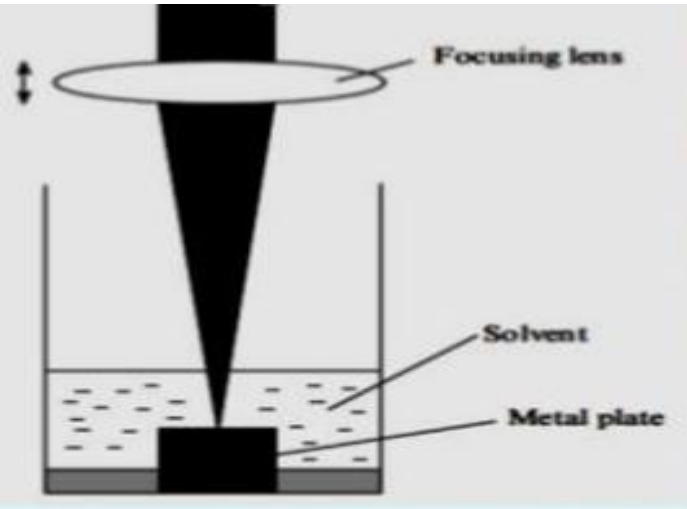

Figure 3: YAG -Laser ablation technique

The main benefit of this laser technology is that in this procedure unblended and beneficial metal colloids are prepared in the absence of toxic chemical agents and this colloid has many advantages in various fields (Tsuji T et al. 2002).

AgNPs of 20-50 nm is prepared in the hydrous medium by laser ablation at 800nm with the help of Femtosecond laser pulses (Tsuji T et al. 2003). Comparison takes place in between nanosecond laser pulses and Femtosecond laser pulses based on:-

Ablation efficiency – nanosecond laser pulses ablation same in water and air but another laser pulse that is femtosecond laser pulse ablation is less in water than in air.

Size of colloid particle – the colloids formed by nanosecond pulses have a large particle size than that of colloids formed by Femtosecond laser pulses.

Formation efficiency – the formation efficiency of nanosecond pulses is higher than that of Femtosecond pulses.

Siegel and colleagues have given evidence of the formation of silver nanoparticles by emitting metal particles explosively into the aqueous medium producing a sputtering sound. This method is a substitute for time taking, a technique related to moisture-based chemical synthesis.it includes a physical accumulation of metallic atoms to glycerine. The round shape AgNPs obtained from the above process and have an average radius of about 1.75with a standard deviation of 1.2.it was noticed that the particle scattering and size dispersion of nanoparticles remain the same for dilute liquid solution in the ratio of 1:20 of glycerol to water (Siegel J. et al. 2012).

Advantage of physical method compare to the chemical method

Uniform nanoparticles can be formed.

In absence of pollutants solvents, the pure nanoparticle is formed.

DRAWBACKS OF PHYSICAL METHOD

- It requires high heating time and a high cost of power.
- The physical technique includes very costly machines to synthesize silver nanoparticles.
- It is not functioning for all the dyes.
- It consists very concentrated mud design.
- It consists short lifetime.

FABRICATION BY CHEMICAL APPROACH

A large number of silver nanoparticles can be formed by reduction method in small time by using different organic and inorganic chemicals. (NaBH4, DMF, sodium ascorbate, sodium citrate, and tollens reagent) can reduce silver ions.

Preparation of Silver Nanocube

Sun and Xia (2002a) have been synthesized cubic AgNPs by using different solutions such as silver nitrate (Polyvinyl pyrrolidone)PVP, but if the ratio increases from 1.5 to 3 0f PVP and $AgNO_3$the product become multiply twinned particles (MTP_s) (Sun, Y. et al. 2002). After that (Im et al., 2005) synthesized cubic nanoparticles by using $AgNO_3$ +ethylene glycol at 14**0**° C in the presence of PVP and HCL then the formation of 25-45nm cubic nanoparticles take place (Im S.H. et al. 2005).

PVP acts as a capping agent which is used to form a cubic structure the shape of AgNPs is determined by the ratio of PVP and silver ions (Tao et al., 2006). The role of HCL is promoting cube perfection and monodispersity (Tao, A. et al. 2006).

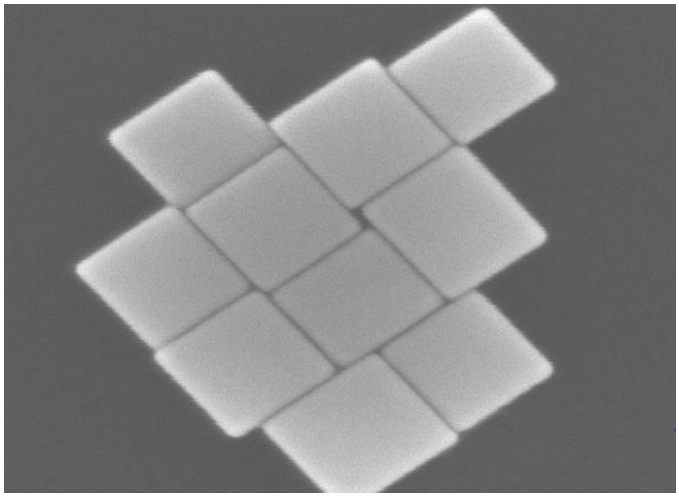

Figure 4: Prepared silver nanocube

Preparation of silver nanorods:

Zhang et al. synthesized silver nanoparticles in the form of the rod (nanorod). Firstly spherical silver nanoparticle seed is taken which is formed by trisodium citrate, silver nitrate, bis (p-sulfonatophenyl)-phenyl phosphine dihydrate dipotassium salt (BSPP), and sodium hydroxide solutions irradiating with 254 nm light.

The nanorod is prepared in the solution containing spherical seed, sodium citrate, silver nitrate solution then illuminate for 24 hours with the help of a bandpass filter then the resulting silver nanostructure parameter can be controlled by photo edited method (Zhang J et al. 2011).

Ojha et al. synthesis the nanorod by using the solution of sodium hydroxide, citrate, silvernitratethen add $NaBH_4$ (ice cold) stir the solution to prepare silver nanorod by the stock solution of ascorbic acid+ $AgNO_3$+ cityltrimethylammonium bromide (CTAB). This stock solution is mixed properly and added three times in the previous seed solution and at the end, a small amount of NaOH solution is added. The large quantity (600±20nm) of nanorod formation occurs and the color of each nanorod depends on the concentration of spherical seed solution (Ojha AK. et al. 2013).

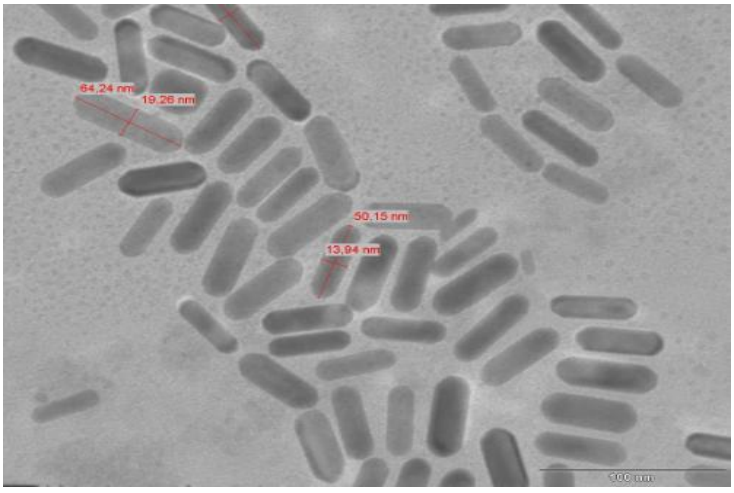

Figure 5: Silver nanorod

Preparation of silver nanowires

Sun et al. studied silver nanostructure which could be changed from nanorod and nanoparticle to long nanowires by this can be done by adjusting the reaction condition which has the ratio of PVP, silver nitrate, seeding condition, and reaction condition then they found the large scale of synthesis of the silver nanowire with a diameter 30-40 nm and length = 50 nm (Gebeyehu MB. et al. 2002).

Li et al. said that the silver nanowire is formed by the polyol synthesis control by just bromide concentration. By adding sodium bromide in $AgNO_3$ in a higher ratio. it leads to the formation of a silver nanowire of 20 nm diameter and a ratio of 2000. (Li B. et al. 2015).

Gebeyehu et al. synthesized silver nanowire by different solution methods. They used a capping agent and the stabilizing agent (PVP), ethylene glycol (reducing agent), potassium bromide salt, and silver nitrate (precursor). The silver nanowire ratio >1000 and diameter 20 nm were obtained by controlling the concentration of $AgNO_3$ and PVP. (Gebeyehu MB et al. 2017).

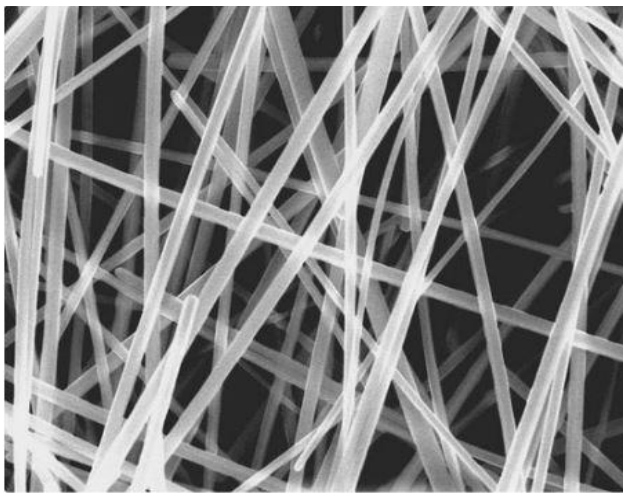

Figure 6: Silver nanowire

Preparation of triangular silver nanoparticles

Zhang et al. have been synthesized the triangular silver nanoparticle by using a different agent. 0.3 $AgNO_3$ add in the solution containing 1.5 M sodium citrate + 0.3 M phenyl phosphine dihydrate dipotassium salt + 0.005 M NaOH mix it and leave it for 8 hours by using a bandpass filter. after some time the mixer is seen in different wavelength ranges. (500, 550, 600, 650) and the formation of triangular silver nanoparticles formed (Zhang J. et al. 2009).

FABRICATION OF SILVER NANOPARTICLES

Reduction by tri-sodium citrate

Dissolve $AgNO_3$ in 500ml water and then heat it at (95-98°C). After that add 5 ml of 1% trisodium citrate in the $AgNO_3$ solution stirring forcefully then the mixture is heated for 20 min till the pale yellow color is obtained. This shows the AgNPs formation and it can change in size when put at room temperature. then washed 3-4 times with distilled water and stored at 4°C to obtained silver nanoparticles. (Bin Xue B. et al. 2015)

Microemulsion method

In this method, the mixture of water, oil, the surfactant is used for the preparation of silver nanoparticles. Some surfactants are used such as sodium dodecylbenzene sulphonate, sodium sulfate, and a nonionic surfactant such as Triton X-100, etc. The surfactant covers water droplets and provides an environment for the formation of nanoparticles. (Wani IA. et al. 2013).

Drawbacks of Chemical method

- The main disadvantage of the chemical method is that it includes highly toxic and costly chemicals which show harmful effects to not only the environment but also to the human body.
- These chemicals are nonbiodegradable and less eco-friendly to the environment.
- The nanoparticles are prepared by this method are not worthy for biological activity.
- Nanoparticles are synthesized in a short time by the chemical approach but they consume high energy, pressure, and temperature.
- Due to these effective intentions, scientists are now focusing on the preparation of AgNPs by plant extraction, bacteria, and fungi using green chemistry.

Characterization

The detection technique of nanosilver particles contains Fourier transform infrared spectroscopy (FTIR), Transmission electron microscopy (TEM), X-ray diffraction (XRD), Nuclear magnetic resonance spectroscopy (NMR), Scanning electron microscopy (SEM), X-Ray Photoelectron Spectroscopy (XPS), Atomic force microscopy (AFM)and UV-Vis spectroscopy. The different parameters such as morphology, particle size, orientation, particle shape, surface area, volume ratio, dispersion of nanotube, nanocomposites, nanoparticles, and crystallinity can be identified by these techniques.

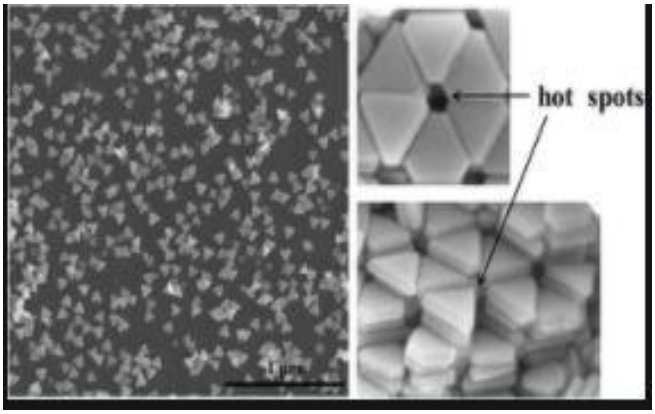

Figure 7: Triangular silver nanoparticle (Bin Xue B. et al. 2015)

FABRICATION BY GREEN APPROACH

Nanotechnology is a new technique by which a large number of nanoparticles can be formed by using various approaches such as biological, chemical, and physical but physical and chemical require high maintenance time and very toxic chemicals for synthesis AgNPs which is not eco-friendly to the environment. So to stop using effective chemicals new method is proposed that is a biological approach that is less toxic and easily available and contains no biological effect. Various using organisms for preparing silver nanoparticles like Bacteria (Nair B. et al. 2002), Plant (Mukherjee P. et al. 2001), Fungi (Chandran S. P. et al. 2002).

A good platform provide by a plant to form low-cost and less effective nanoparticles these nanoparticles have more competitive capability or feasibility as compare to that nanoparticle prepared by microorganisms. (Singhal G. et al. 2011). Nanoparticles can be prepared by using different plant extracts with require less pressure, temperature and have a less biological risk to the human body (Gilaki M. 2010).

Nowadays, scientists are using the biological method in which plants act as a source of nanoparticles such as aloe barbedencis, solanum nigrum, Clitoria ternatea, etc plant extracts processed with silver nitrate solution to obtain silver nanoparticles. (Lal and Nayak, 2012), Lal, S.S. et al. 2012).

The required amount of silver nanoparticles can be produced by using plant extracts that can reduce Ag ions in large amounts (Singh and Srivastava, 2015) (Singh A, K et al. 2015).

Nanoparticles obtained by large active research technology that is nanotechnology in medical specialty show various properties depend on characters related to structure, dimensions, and distribution.

Silver nanoparticles have various pharmaceutical applications because of their characteristics electronic and photovoltaic features.in contrary to this, AgNPs have a greater surface area and small size, which makes them effective against bacterial disease this shows its antibacterial property. synthesis of AgNPs can be done by reacting $AgNO_3$ with the fruit extracts such as tomato and guava and then AgNPS are obtained as a result of the above reaction. The obtained silver nanoparticles have versatile features, acting against both Gram-positive (s.aureus) and Gram-negative (e.colli) making it a broad spectrum substance. The AgNPs are also used in pharmacy, in the treatment of burn care, and other health issues. These nanoparticles can also use in daily life in liquid detergent, body wash, shampoo, and in many more things (Bawsker et. al. 2015),Bawskar M et al. 2015). Cacumen Platycladi extract is used for the formation of silver nanoparticles which shows different results by enhancing the concentration of silver nitrate and characterized in TEM, X-ray, UV-vis. This results in creating changes in the size of AgNPs and leads to the broadening of the surface. (Huang J. et al. 2011)

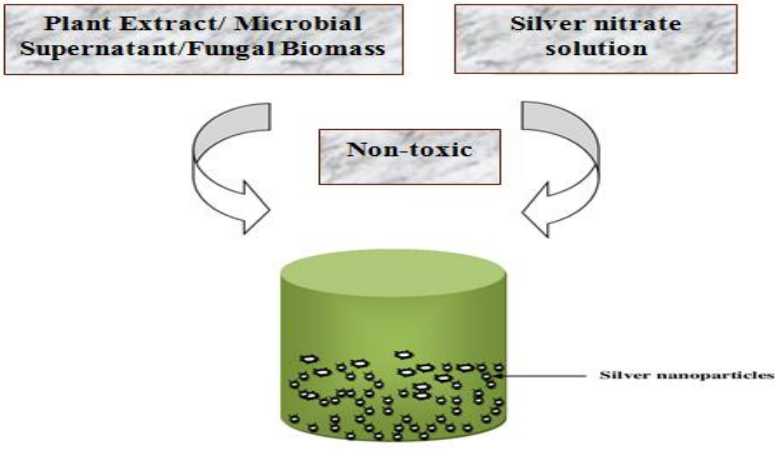

Figure 8: Prepared silver nanoparticle

Green approach for the preparation of silver nanoparticles by using solanum nigrum and Clitoria ternatea plant extract

Solanum Nigrum

Clitoria Ternatea

Biosynthesis of silver nanoparticles by using plant extract required Clitoria ternatea and Solanum nigrum fresh leaves and 0.1 M $AgNO_3$ solution**.**

PREPARATION AND COLLECTION OF PLANT MATERIALS

In the first step fresh leaves of two plants Solanum nigrum and Clitoria ternatea was collected than with the help of the tap water rinse the leaves 2 or 3 times and one time with sterile water to remove the waste debris from leaves then 20 grams of leaves is chopped and add it to the 100ml distilled water and stir the solution for 1 hour at 60-degree temperature after the heat the solution and leave the solution for cool and after some time resulting solution is filtered with the help of wattman filter paper and the resulting filtrate was collected**.**

PREPARATION OF SILVER NANOPARTICLES

In the second step, 0.1 M of silver nitrate solution is formed for the preparation of silver nanoparticles. Now, the leaf extract of two plants is taken (5ml) and added 45ml silver nitrate of 0.1 M solution in it leave the solution at room temperature for the bioreduction process the color changes from colorless to yellowish-brown this indicates the formation of silver nanoparticles. (Singhal G. et al. 2011).

Characterization Techniques

X-RAY DIFFRACTION

XRD is utilized to analyze the size of the particles and crystalline property of AgNPs.For the XRD analysis silver nanoparticle thin film is prepared for x-ray studies. the size of nanoparticles can be identified by the debye scherrer equation**.**

$$D = \frac{k\lambda}{\beta cos\theta},$$

K = constant, β= width at half maxima, D = thickness of the nanocrystals, λ = wavelength of x-rays, θ = Bragg angle,

The crystalline property of AgNPs analyses with the help of x-ray diffraction peaks width. (Prema P. 2010).

FTIR (FOURIER TRANSFORMS INFRARED SPECTROSCOPY)

FOR FTIR analysis centrifuged solution of silver nanoparticles is required by centrifuging it at 1000 rpm for half-hour are formed. FTIR is used to analyze the different biomolecules, functional groups, and organic compounds responsible for AgNPs and the dry pellet of silver nanoparticles. In this technique, the pellet of silver nanoparticles is washed three times in deionized water so that the pellet becomes free from all the enzymes and protein that are not attached with silver nanoparticles and dry it with the help of a vacuum drier**.**

UV- VISIBLE SPECTROSCOPY

The absorption peak of the reaction was analyzed by spectrophotometer with a speed of 200nm per min and resolution between 200-1000nm. The reaction between leaf extract of Solanum nigrum and Clitoria ternatea and metal ions development was controlled by UV visible spectra at room temperature with different wavelengths 350 -800nm. By the reduction process, the silver nanoparticle can be synthesized in an hour and a solution of silver nitrate is used to control and maintained the reaction. (Shankar S.S. et al. 2005).

SCANNING ELECTRON MICROSCOPE(SEM)

For the sem estimation, the small carbon-coated grid is required to prepare a thin film of silver nanoparticles by dropping some amount of sample solution on the grid. The more amount of water can be soaked from the grid with the help of blotting paper and then the thin film is dried and analyzed by SEM and Sem is also used to identify the morphology of nanoparticles (Savithramma N. et. al 2011).

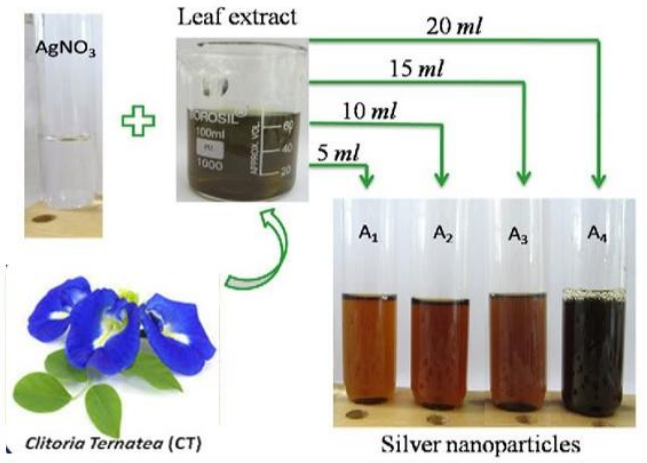

Figure 9: Silver nanoparticle using plant extract

RESULTS

For the computation of the size of silver oxide obtained from the above experiment are inevitably exposes to XRD analysis X-ray diffraction pattern of prepared silver nanoparticles from leaf extracts of Solanum nigrum and Clitoria ternatea indicated by the a and b two figures the sharp peak shows that the shape of nanoparticle is spherical and some different peaks of intensity shown by two leaf extracts such as 28, 32, 39, 45, 55, 57, 65, 69, 75, and 77 in Solanum nigrum 28, 33, 38, 44, 46, 55, 58, 65, and 77 in Clitoria ternatea**.** nanoparticles size can be identified by the debye scherrer equation. The silver nanoparticles obtained from Clitoria and Solanum leaf extracts approximately having a size of 20nm and 28nm.

Fourier transforms infrared spectroscopy is utilized to determine the functional groups and biomolecules fix with the AgNPs so the band of absorbance of Solanum nigrum was found at 2933.88 cm−1 assigned to C–H (s) stretch, 1394.44 cm−1 assigned to C–H alkenes stretch,3317.34 cm−1 assigned to O–H (s) stretch,1191.93 cm−1 assigned to C–N amines stretch,1122.49 cm−1 assigned to C–N amines stretch 1191.93 cm−1 assigned to C–N amines stretch, and 752.19 cm−1 and 655.75 cm−1 assigned to C–H alkenes stretch. and the band of absorbance of Clitoria ternatea was found at 1614.31 cm−1 assigned to C=C aromatic stretch,1191.93 cm−1 assigned to C–N amines stretch,3317.34 cm−1 assigned to O–H (s) stretch,752.19 cm−1, and 655.75 cm−1 assigned to C–H alkenes stretch.

UV-Visible spectroscopy shows the absorption peak of Prepared nanoparticles. The UV spectra of synthesized silver nanoparticles by using Solanum nigrum leaf extract shows the higher absorption peak at 440 nm and the other leaf extract that is Clitoria ternatea shows the higher absorption peak at 420 nm

Scanning electron microscopy (SEM) micrograph exhibits that the formation of silver nanoparticles decreases due to acidic conditions and the formation of silver nanoparticles increases due to basic conditions. The effect of PH on the size of nanoparticles is also determined by this technique. This shows that the low level of PH (PH=4) is responsible for the formation of large silver nanoparticles, AT high level of PH(PH=9) is responsible for the formation of highly dispersed small silver nanoparticles, and at neutral PH(PH=7) is responsible for the formation of normal size nanoparticles.

BACTERIA ACT AS A MEDIUM FOR GREEN SYNTHESIS

Bacteria also play an important role in the synthesis of silver nanoparticles by producing inorganic intra and extracellular materials. This production leads to an increase in the AgNPsSynthesis in different factories related to green synthesis. Some bacteria are said to be Silver resistant bacteria and silver consists of different properties related to biocidal properties (Slawson R.M. et al. 1992). Silver nanoparticles are also suggested for industrial use for the recovery purpose from ore materials because silver has accumulation properties to the cell wall and can assemble approx 25% biomass of AgNPs. (Pooley F.D. 1982).

Some prokaryotic bacteria are utilized for the production of metallic nanoparticles. Such as Pseudomonas stutzeri AG259, which acts as silver resistant bacteria cultured with the help of silver nitrate solution at high concentrations. The result of using this bacteria is that 200 nm diameter of the silver nanoparticle is formed due to high accumulation of silver by the cell and deposition of silver occur in the large amount. (Klaus T. et al. 1999). Another bacteria which is Proteus mirabilis PTCC 1710 give remarkable results utilized for silver nanoparticle synthesis. At the time of incubation, nanoparticles production is based on the type of various broths which can promote extracellular and intracellular growth. Bacteria-based green synthesis can form large-scale, easily synthesized less expensive nanoparticles. (Samadi N et al. 2009). The main disadvantage of bacteria based green synthesis are :

The rate of production or preparation of silver nanoparticles is very slow. Little amount or no more shape size of nanoparticles can be produced as compared to other chemical and physical method. Due to this reason fungi based green synthesis can be done or investigated for the AgNPs production. (Kharissova O.V et al. 2013).

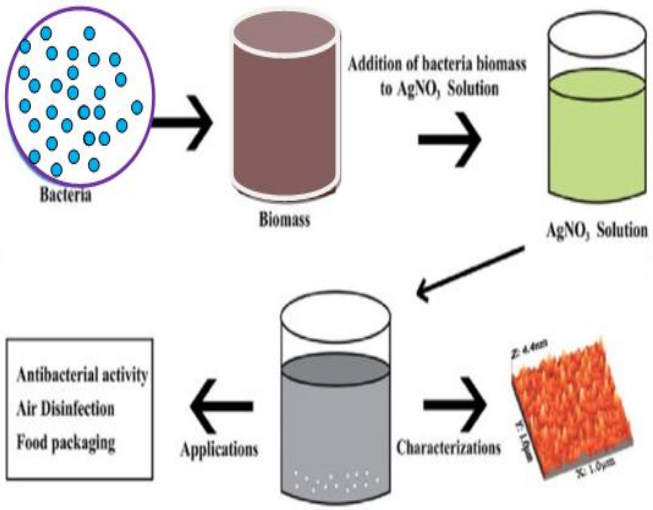

Figure 10: Preparation of Ag-NPs by using bacteria (Muhammad Rafique M. et al. 2017]

FUNGI ACT AS A MEDIUM FOR GREEN SYNTHESIS

Fungi also act as a medium for synthesis of silver nanoparticle better than the bacteria and easily hold in the laboratory for the synthesis of metallic nanoparticle and also because of large binding capacity, accumulation capability, high tolerance power fungi is used in high amount for formation of stable high quantity silver nanoparticles (Murali S. et al. 2017). The process of making AgNPs by fungi is different. Reduction of silver ions can take place by using enzymes that are secreted by the fungi that persuade the nanoparticle formation (Mandal D. et al. 2006).

In the 20th century, the first synthesis by using fungi green synthesis for the preparation of metallic nanoproducts occurred. Verticillium fungi are used to form the 25±12 diameter silver nanoparticles (Mukherjee P. et al. 2001). By using Verticillium fungi at the time of disclosure of fungus to silver nitrate solution the silver ions reduce and the formation of approx 24nm silver nanoparticle takes place. The surface below the fungal cell is the place where the monodisperse good spherical shape nanoparticles are synthesized (Ahmad A. et al. 2003).

Klaus et al. 1999, works on AgNPs synthesis. They found that the nanoparticle formed by bacteria having different shapes like hexagonal, spherical, and triangular. After that in the case of fungi based synthesis surface of mycelia is considered for the nanoparticle synthesis which is absent in solution then it was found that in the 1st step because of electrostatic interaction between carboxylate ion (anion) and silver ions (cation) on the surface of mycelia is considered for the adsorption of silver ions and at last the reduction Ag ions by using enzymes shows the formation of silver nuclei. In comparison with bacteria and fungi, fungi lead to the large production of nanoparticles and also secrete a high amount of enzymes and protein which is used to prepare the silver nanoparticle in bulk quantity. (Mukherjee P et al. 2001).

Ahmad et al. 2003 use the eukaryotic system for the synthesis (extracellularly) of AgNPs and said that for the reduction mechanism secreted enzymes are utilized (Ahmad A. et al. 2003). The nanoparticle is synthesized extracellularly having an advantage over the intracellular synthesis in that it does not attach to the biomass which leads to the increase of biosynthesis approach of making AgNPs as compared to chemical synthesis which includes oxide, nitrides like chemical contexts. (Balaji D.S et al. 2009, Durán N. et al. 2005).

Another example of nonpathogenic fungi i.e. white-rot fungus is also included in the production of silver nanoparticles in high amounts. (Vigneshwaran N. et al. 2006). Another fungus i.e. Aspergillus fumigatus which can be synthesized stable and disperse AgNPs within approx 10-15 minutes. (Bhainsa K. C. et al. 2006). A. flavus fungi used recently to form the antibiotic combination silver nanoparticle to increase the biocidal property in apposition to multi-drug resistant bacteria. (Naqvi S. H. Z et al. 2013). Like fungi, yeast also takes place in the green synthesis of silver nanoparticles. (Mourato A. et al. 2011). The first yeast is MKY3 silver tolerant yeast stain is utilized for the extracellular synthesis. The nanoparticle which is prepared y using yeast is easily separated when different thawing is used. (Kowshik M. et al. 2003).

The yeast is found in grocery stores for commercial use is not considered or included for nanoparticle synthesis because it takes time or more steps to cultivated so to ignore these steps and make the process easier doesn't consider for AgNPs production. (Saravanan M. et al. 2014). Biosynthesis done from prokaryotic to eukaryotic the eukaryotic autotroph enhances the chances of biosynthesis in a large amount. As we differentiate to another biological method for example Sargassum wightii marine algae are used to form the very stable metallic nanoparticles. (Singaravelu G. et al. 2007). Silver nanoparticles can be formed by all these methods and considerable results are also shown by collecting data with the help of all the published articles and get different results. Due to the presence of different optical properties, chemical and physical properties such as small size high conductivity electricity, and imaging sensing help in predicting cancer cells and some biosensing platforms. AgNPs are also utilized as a carrier system for drug delivery and cancer treatment. (Huy Q.T. et al.2020)

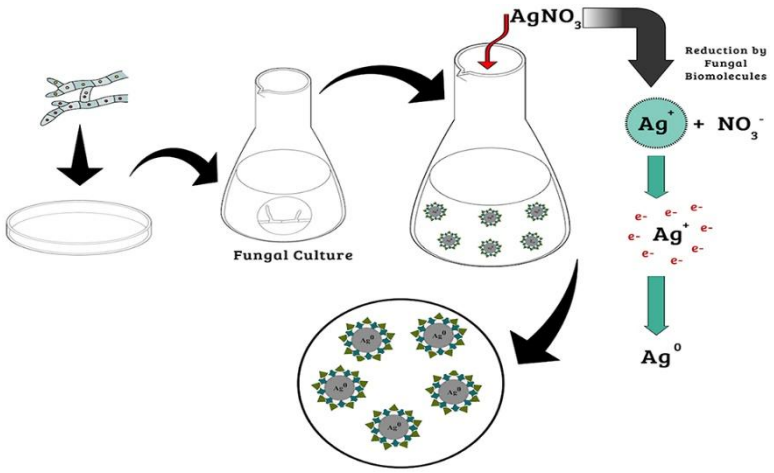

Figure 11: Mechanisms of Bio preparation of silver nano products.(Guilger Casagrande, M. et al. 2019)

ADVANTAGE OF GREEN APPROACH

- Eco friendly.
- It does not require high pressure, temperature, and toxic chemicals.
- An easy method to prepare nanoparticles in bulk quantity.
- Eliminate the formation of toxic nanoparticles.
- The fast approach of synthesis nanoparticles as compared to physical and chemical.
- No need for large processing during synthesis.
- The green approach lowers the cost of culture media and the separation of microorganisms.

APPLICATION OF SILVER NANOPARTICLES

Metallic nanocatalyst consists of various applications due to their different shapes and size of materials like in the form of a rod, wire-like nanofibre, and quantum dots. Silver nanoparticles show different electrical, optical properties which increases the high range of attention in the biomedical field. Nowadays, silver nanoparticles gaining Importance in nanomedicines, due to their morphology and researches.

Many scientists studied silver nanoparticles and investigated the AgNPs because to get the increased properties. Silver nanoparticles are used in solar cells as plasmonic light traps. Because of these properties silver nanoparticles become valuable male significance importance in other applications in nanomedicines.(Butun S et al. 2011, Harish S. et al. 2011).

A silver nanoparticle is become a popular metallic nanoparticle due to its antifungal properties and it is widely used in wound healing, disease treatment, food packaging, soap detergents, and cosmetics (Botta R. Et al. 2013). Different – different % of the silver nanoparticle is used in our daily life products 52.61% household equipment, 4.02% in medicines, 3.21%, and 11.65% in other uses. Silver nanofibre can catch small particles easily because of the big surface area and sticky nature this property makes the nanofibre good to utilized for filtration purposes (Zhang T et al. 2014). Out of all these silver nanoparticles show, another various application in different medicinal use and therapeutic application in nanomedicines is discussed below.

APPLICATION IN CANCER TREATMENT

In cancer therapy, the nanoparticle can be used based on two purposes that are detection and therapy purpose. Silver nanoparticles can control gene expression and can make changes to more than 1000 genes. They have the potential to influence intracellular function. Some genes are histones, metallothionein were play an important role. One mechanism that is autophagy induced cell death is used nowadays, for cancer therapy which acts as an anticancer activity for silver nanoparticles. Silver nanoproducts are also used to insert the autophagy mechanism in the human cell from ovarian cancer cell to encourage cell death by the accumulation of autophagolysosomes. The two functions performed by this anticancer autophagy mechanism is that in a low level of autophagy cell survival is occurred and at a higher level it can cause cell death. That's why nanoparticle-induced cell death can be occurred by using inhibitors or autophagy blockage and small interfering RNAs (siRNA) (Jeyaraj M. et al. 2013).

Therapy approaches related to photo is utilized by nanoparticle for detection, treatment, and preventive measures. The different small structures of the nanoparticle can be used easily to destroy the cancer cell at a low level of energy irradiation. Scientists developed Au- Ag shell core nanostructure photothermal therapy due to high irradiation cell death property by this nanostructure easily kill the cell with high power and particularity which based on sensitive and particular recognize aptamer. Nanoparticles have several therapeutic applications such as radiation enhancers,

chemotherapeutic agents, act as a carrier in drug delivery and photodynamic therapy in various laboratories. Photodynamic therapy plays an important role or is widely used for the treatment of cancer. Nanomedicines related to phototherapy is become more significant and also act as a nanocarrier for drugs for cancer surgery rather than other therapy approaches. There are some drawbacks while using nanomaterials is that it involve a limited amount of carrying ability, increase some EPR effect, physiological barriers, manufacturing and controlation issue, and some nanomaterials variations. (Satyavani K. et al. 2013)

THERAPEUTIC APPLICATION OF SILVER NANOPARTICLE

Nowadays, therapeutic application of silver nanoparticles increases in many different fields of nanomedicines some applications related to anticancer agents are discussed below:

Silver nanoparticles act as anti-angiogenic agents

The angiogenesis property which means the new blood cell is formed by pre-existing vessels acts as an important participant in the function of cancer and other diseases so to inhibit this property silver nanoproduct is utilized. Eom's group found that in vitro the silver nanoparticle, PEDF, and the antiangiogenic molecule are used to block PI3K/Akt phosphorylation in bovine retinal epithelial cells (BREC) and stop the harmful effect of angiogenesis induced vascular endothelial growth factor (VEGF), (Gurunathan S.et al. 2009). Some nanoparticles such as AgNps act as extracellular release drug delivery after entering in tumor cells attached with outer membrane or interiorize into the microenvironment related to tumor cells. NPs are also utilized for predicting, sensing, and in photodynamic therapy to destroy abnormal cells with the help of light-sensitive medicine. Raja G. et al. 2020 A study said that silver nanoparticles can stop the formation of new blood cells in vivo and in vitro. Dalton's lymphoma ascites. Another study demonstrated that the cytotoxicity of the silver nanoparticle can be seen in the apposition of DLA (Dalton's lymphoma ascites) cells in vivo and in vitro. As we compared to other tumor cells tumor mouse model survival time is enhanced by about an average of 50%. (Sriram M.I et al. 2010)

Application of silver Nanoparticle

In Leukemia

Leukemia is a disease consists a group of cancer occur in the bone marrow and increase the formation of abnormal leucocytes and decrease the formation of normal blood cells lead to the occurring of anemia. Many studies revealed that some cytotoxic effects against leukemia cells can be shown by silver nanoparticles such as K562 cells, Jurkat. Which helps to reduce the effect of leukemia. Nowadays, Guo et al establish that AgNPs coated with poly(N-vinyl-2-pyrrolidone (PVP) could stop the function of AML cells involving separation of low concentration of AML cells from the patients gives the good approach for the therapy of AML cells (Guo D. Et al. 2013). Another study revealed that silver nanoparticle acts as a carrier for the k562 cells to enter in the endosomes in the form of drug-dependent treatment manner (Guo D, et al. 2014).

In Breast Cancer

In MCF7 breast cancer cells, the silver nanoparticle can show the cytotoxic effect which is dose-dependent is observed due to the injection of apoptosis and having a concentration approx 50% of LD50 of 3.5 ng/mL and LD100 of 14 ng/cell growth inhabitants (Franco-Molina M.A. et al. 2010). Gurunathan et al. establish that MDA- MB 231 cell death with the help of ROS generation is induced by silver nanoparticles which results in the DNA fragmentation, and activation of caspase 3 (Gurunathan S, et al. 2013). Further work of the same group said that the cytotoxic effect with apoptotic features is shown by single-crystalline AgNPS (Gurunathan S, et al. 2013).

In Lung Cancer

Cytotoxicity in the lung cancer cell can be exhibit with the help of silver nanoparticles.Foldbjerg et al found the mitochondrial function reduction which is(dose-dependent) in the A549 cells of the human alveolar cell line. It was said that silver nanoparticle is taken from the cell which results in enhancement of the ROS production and leads to the apoptotic and death of the necrotic cell (Foldbjerg R, et al. 2011). Another Nazir et al exhibit that the exclusive anticancer property of silver nanoparticles is apposite to the squamous cell lung carcinoma cell line i.e H157 accompanied by IC50 of 3.6μM (Nazir S, et al 2011). AgNPs are also shown energy to another cancer type such as pancreatic cancer its very dangerous disease in this patient survival is very unsuitable. Colloidal silver is first utilized against pancreatic cancer. By using silver nanoparticles patients' condition may be improved and get the best results for pancreatic cancer patients (Foulkes R. et al. 2019).

In Wound Healing

Wound treatment in various clinics can be done by using silver nanoproduct which is investigated by Robert Burell. Some involving wounds are- chronic ulcers, toxic epidermal necrolysis, burns, etc. Silver nano dressing which is NCP-loaded is more significant rather than other wound dressing because it consists of healing properties much better and decreases healing time approximately 3.35 days and also enhances the cleaning of polluted or wound from bacterial infection as compared to silver sulfadiazine without causing the major effect. This wound dressing becomes very supportive for infection-related skin problems (Maneerung T. et al. 2008, Singh R. et al. 2014).

CONCLUSION AND FUTURE ASPECTS

The conclusion of this review article is about silver nanoparticle synthesis and the utilization of silver nanoparticles in different fields of nanomedicines. Due to the presence of different properties of AgNPs such as antibacterial, anticancer, because of this unique ability, it gains more attention in the fields of therapies. Different shapes of nanoproducts in the form of rod cubes and triangular and wire can inject easily into the human body to treat the problems related to health.it can be synthesized from physical chemicals and environmentally friendly products with the help of green chemistry. Nanosilver products have some harmful effects on the function if changes are occurring in the fabrication process. A high concentration of silver can affect the human body and create large problems if comes in contact with the environment. So low concentration is used to inject into the human body. Silver nanoproducts exhibit therapeutic application and cancer treatment applications. AgNPs have more ability so that they can enhance their application demand for the future outlook. Scientists can work in many laboratories with silver nano products to form the vaccines and medicines to treat the diseases related to bones and human health. In the future improvement of nanoproducts can be easily occurred by protecting them from contaminated particles and utilized for future surgeries.

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