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A review on preparation methods of SNPs and their biomedical applications

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Abstract

Researchers have identified Silver Nano Particles (SNPs) as a key area of interest because of their unique shape and size dependent biomedical properties. They have discovered and invented a variety of methods for the synthesis of SNPs such as microwave irradiation techniques, laser ablation synthesis, biological synthesis, photochemical synthesis and chemical synthesis etc. In this review paper we overview the preparation of SNPs through various synthesis methods and also their applications in the bio-medical field. The main aim of this paper is to keep up to date with the myriad ongoing synthesis methods of synthesis of NPs and also examine their applications especially in the field of medicine.

Silver Nano Particles (SNPs)

Silver (Ag) is a white colored, lustrous looking, physically soft, transition element metal having high thermal and electrical conductivity. It has been used by humans earlier than the recorded history due to its ornamental, medical and therapeutic benefits even before realizing that microbes are the causative agents of infections. It is used by people in many forms such as solutions, foils, coins, vessels, sutures, and in colloids such as lotions, ointments etc. It is one of the most prominent therapeutic elemental agent in medicine for surgical infections and infectious diseases. The tangible advantages of silver have a bigger weightage than the intangible risk factors [1].

Nanoscience is a novel multidisciplinary subject that depends on the basic physical and chemical properties displayed by nano level objects [2,3]. Nanoparticles have been shown to display amazing electro-magnetic, surface optical and chemically catalytic characteristics than the macro bulk material owing to their extremely low volume to surface area ratio [4,5]. Metal nanoparticles such as silver show different colors due to their Surface Plasmon Resonance (SPR) phenomenon. It is a group oscillatory behavior of the free electrons of the metal nanoparticles having the same frequency of the light wave interactions, resulting in resonance, causing the SPR band to form in the infrared and visible region [6]. Nanoparticles, especially the metallic ones, whose production can be done through various methods, the usual ones being physical and chemical methods. The above-mentioned methods produce high purity, well-defined nanoparticles, but the reagents used in the synthesis are hazardous, energy consuming, expensive, toxic and not suitable for physiological or ecological applications. Research regarding the synthesis of metal nanoparticles was extensively covered in the past three decades, but research of nanosynthesis , based on plant extracts, bloomed only in the last ten years [7-13].

Silver nanoparticles are finding themselves in the limelight due to their biological, chemical and physical properties that contributes to the bactericidal and fungicidal effects, catalytic activity and finds applications in nanobiotechnological research [14,15]. Doctors are beginning to use them in wound dressings as anti-microbial agents, in topically applied creams used to prevent wound infections, and even finds success in use as anticancer applications [16-20].

Preparation of SNPs

Different strategies are used for the preparation of nano structures that are mostly metal, that should be usually controllable regarding their shape and size, high yield with less waste of products, cost effectiveness and environment friendliness. Figure 1, Comprises of various planning methodologies for SNPs. Metal nano structures exhibit huge abundance of plasmon excitations for example researchers are now showing increased interest in SNPs due to this phenomenon, which is in the range of visible spectrum and has been marked for potential use in many future technologies. Here, this paper will examine all the most reference synthetic processes involved in metal nanoparticle preparations, especially that of silver (Ag).

Chemical reduction synthesis

One among the most frequently used processes is the technique of chemical reduction used to synthesize SNPs using organic and inorganic reducing agents. Different reducing agents like tri sodium citrate, sodium borohydride, ascorbic acid etc are used in reducing Silver ions (Ag+) to metallic Silver (Ago) after which cluster formation takes place. Therefore, colloidal SNPs are formed from the afore-mentioned clusters in aqueous or non-aqueous solutions.

Research has found that it is necessary to use agents of protective nature to stabilize nanoparticles during the process of formation and that these agents protect them by being absorbed or bound to the NPs

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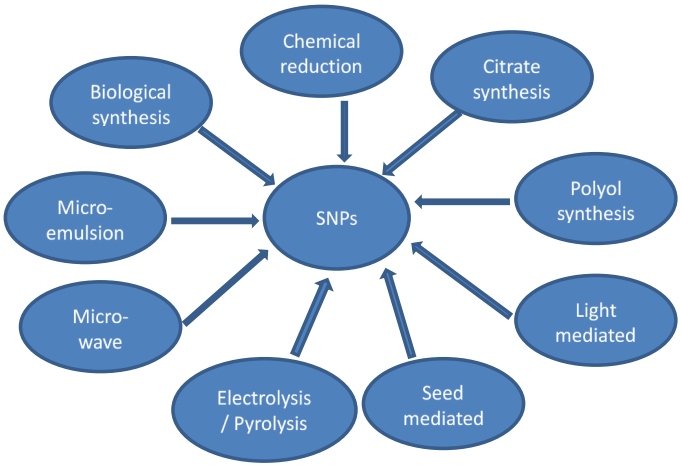

Figure 1. Various planning methodologies for synthesis of SNPs.

surfaces preventing their clustering. The existing compounds that lower surface tension are termed as surfactants, these have a stabilizing effect which comprises characteristic abilities to stabilize particle growth, meanwhile reacting with the particulate surface. Using these fortifying agents protects the particles from clustering and helps to preserve their shape and size and from the loss of particles surface properties.

The shape and size of the metal nanoparticles critically determine the optical characteristics. The one of a kind plasmonic characteristics of metal nanoparticles are largely influenced by the controlled morphology. So far, different techniques have been tried and adopted for the production of these NPs with controlled shape and size [21-23]. Usually, the initial form of silver ion (Ag^+) is mixed with reducing agents while in the vicinity of a fortifying agent which controls the shape and size of the metal NPs. Previous scientific research has shown that the preferred precursor is silver nitrate and has been broadly used because of its easy accessibility and affordability. There are myriad reducing agents that are abundantly used to reduce silver ions (Ag^+) present in the solution to individual silver atoms which come together to form agglomerates and consequently become SNPs [24-25] Meanwhile, fortifying agents are added to stabilize and control the desired morphology of SNPs.

N_2H_4 can reduce silver nitrate ($AgNO_3$) through a one pot technique of reduction in presence of water (H_2O) and sodium ethanoate (CH_3COONa) at 250°C for 120 – 180 minutes with water as the solvent being utilized [26]. The creation of SNPs (4-8 nm) with size as the regulation parameter was done using a modified version of silver perchlorate ($AgClO_4$) which was reduced by sodium borohydride ($NaBH_4$) without using any agents to stabilize [27]. The time duration of synthesis within 24 – 48 hours was found to be a major factor in determining the size of SNPs mediated by polyethylene glycol and along with the use of β–D–glucose at 450°C [28]. The chitosan stabilized SNPs have been produced using γ – rays.

Citrate reduction synthesis

A frequently used method for preparing silver colloidal solutions is citrate reduction of silver (Ag^+) ions because it doesn't require intense laboratorial skills [29-31]. This method was first introduced in 1982 by Lee and Meisel [32]. In this method SNPs are created when a predetermined amount of sodium citrate is put in a liquid state solution of silver nitrate ($AgNO_3$) which was boiling and kept for a minimum of 60 minutes. Though this method is quite easy it didn't result in regulated size of NPs. The final product exhibited a very broad range of size from 20 - 600 nm. Nevertheless, pH regulation is a critical factor, since only little shape controlled techniques had been examined by earlier researchers by regulating pH with values such pH = 11.1 for spherical shape and rod like particles and pH=5.7 for a triangular shape [33,34].

Polyol synthesis

A broadly well-known and frequently used technique to synthesise broad range of SNPs [35-39]. Usually, the creation of nucleation and growth towards SNPs happens because of the introduction of silver salt capping agents and precursors. The silver (Ag^+) ions found in the solution are reduced by the commonly used reducing agents such as 1, 2-propylene glycol, 1,5-pentanediol or propylene glycol. The probable regulation on the ultimate reaction product is influenced by reaction variables such as concentration and temperature.

Light mediated synthesis

NPs are manufactured by the application of light irradiation in this method. With the source of light acting as a reducing agent, a direct laser irradiation or ablation was conducted on the metal salt solution in aqueous form with the surfactant present to fabricate the size and shape spread of SNPs [40,41]. This coherent light sources is also used to change the metal nanostructures by causing the silver nanospheres to melt into silver nanoplates [42-47]. This method is called as tailoring with light. So far, researchers have had great success for producing good, really desirable and properly regulated SNPs.

Seed mediated synthesis

Over the previous decade another method that is gaining a lot attraction to produce silver nano particles is seed assisted synthesis where nano crystals function as seeds for future growth. The advantages of this technique over final product morphology is profound [48-51]. For instance, Xia et al created, in 2010, silver nano tubes by making use of cubic or spherical shape single crystal seed for a particular length of edge ranging from 30-200 nm.

Electrolysis and pyrolysis synthesis

From the analysis of literature it was found that only a few scientific reports available explaining the usage of electro-chemical technique for the production of SNPs. As an example, silver ions (Ag^+) were reduced with polyvinyl pyrolydone present using electrochemical technique, with platinum plate of 1 cm radius working as anode and titanium electrode working as cathode to produce silver (Ag) NPs which were in spherical in shape. There exists another method comprising of spray pyrolysis for which an average grain size of 100 nm of silver nano powder was found in the synthesis. Of many synthesis processes, electrolysis and pyrolysis methods are judged to be eco-friendly as there is no toxic or hazardous reducing agents involved in the production of these NPs [52,53].

Microemulsion synthesis

Homogenous regulation adhering SNPs can be created using micro emulsion method. The special separation of reducing agent and silver precursor in two phases that cannot be mixed at the start of process is the basis for the SNP preparation in two phase aqueous system that is organic. The rate of interaction amongst reducing agent and silver precursor is affected by the interface between the two solutions and the strength of interface movement between two phases, which is the process assisted by alkali ammonium quaternary salt. The surface of the SNPs being covered with stabilizer molecule which happen to be found non-polar liquid solution and moved to the organic medium with the

help of the inter-phase transporter results in the silver cluster forming at the inference to be stabilized [54]. Greatly hazardous organic solvents being utilized is one of the major drawbacks.

The end product must be bereft of these solvents and huge amounts of surfactants by segregation. For example, Matin et al., [55] found that there was no requirement to segregate the prepared, from the reaction mixture when they utilized dodecace as the oily phase. The surface of polymeric substrate was wetted without any clustering by colloidal SNPs made in non-aqueous media because conductive things are distributed quite well in a low gaseous pressure organic solvent. These organic reactions that have been conducted in non-polar solvents are best catalyzed by the beneficial applications of SNPs as catalyst. During practical applications, these SNPs are supposed to be moved to variety of physicochemical changes as one of the main criteria [56].

Microwave-assisted synthesis

A method with good prognosis for creation of SNPs is microwave-assisted synthesis. Studies have shown that this method consistently yields SNPs with narrower size distribution, higher degree of crystallization and smaller sizes as compared to conventional oil baths [57]. Along with the prevention of the clustering of NPs formed microwave heating has reduced energy usage, greater product yields and shorter time of production [57]. This technique with help from non-hazardous media eliminates the usage of oil baths tremendously decreases the chemical waste and time duration of reaction in many chemical alterations and many organic syntheses [58]. Carboxymethylselilo sodium can be used as a stabilizing and reducing agent for the synthesis of SNPs by this process route. There were no visible variations noticed and the so produced SNPs were stable and uniform at room temperature for 2 months [59]. It was also reported that there was the creation of ethylene glycol and polyvinyl pyrrolidine in the presence of platinum seeds [60].

Biological synthesis

It has been found from recent research that microbes such fungi, bacteria and certain algae have great capability for the synthesis of metal Nps such as Cadmium Sulphide (CdS), Silver (Ag), Zirconia (ZrO_2), Gold (Au), Titanate, Titanium (Ti)/Nickel (Ni) [61-67]. This method provides good regulation over size spread of nanoparticles and is also an eco-friendly and non-hazardous process route for production NPs. For instance, less than 200 nm sized NPs of silver (Ag) were produced using bacteria.

Applications of SNPs in medical biology

SNPs has found increasing use as an attractive application for medical requirements because of their exclusive characteristics like their quantum properties, good surface to mass ratio which is greater than that of other particles and the capability to adsorb and transport other compounds such as proteins, drugs and probes. The field of NPs is being explored continuously in an exponential manner and it is amazing to find that SNPs are receiving the greatest amount of attention. This is inparticular due to huge utilization in electronics, photonics, sensing, catalysis, imaging, drug delivery and environmental cleanup [68-70]. Figure 2. presents the various applications of SNPs in the field of biomedicine.

Catalysis

The usage of nanoparticles as catalyst is a quickly growing field in nanoscience and technology. The characteristics of noble SNPs make

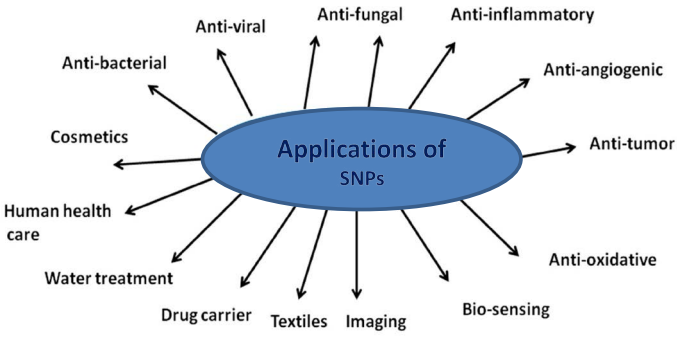

Figure 2. List of applications of SNPs in the field of Biomedicine.

them the best materials for nano-catalysis. Especially where selectivity and reaction yield depend on the properties of catalyst surface. They exhibit greater turnover frequencies as compared to bulk materials because of lower volume to surface area ratio. For instance, we know that in the decomposition of hydrogen peroxide to Oxygen the catalytic properties of Silver are quite useful. In addition, noble metals are also involved in catalysis of luminal hydrogen peroxide systems. It was seen that the addition of silver, gold colloid highly improved the chemiluminescence emission coming from luminal H_2O_2 systems [71]. Also popular is the utilization of silver in the catalysis of ethylene oxide from oxidation of ethylene and formaldehyde from oxidation of methanol. But, something that piques greater interest is that the nanoparticles show shaped regulated catalytic activity. When benzene hydrogenation occurs in the presence of platinum catalyst we can notice shape regulated catalytic characteristics [72].

Drug delivery

Many researchers are of the opinion that SNPs are ideal for drug delivery scaffold because of its non-immunogenicity and its non-toxicity. It is also marked as a viable vehicle for drug delivery because of its functionalization property. It was found that this mechanism released of multiple drugs in a well-regulated manner. These researchers also showed that nanoparticles of various shapes react to different infrared frequencies [73].

Cancer therapy

As we have already seen nanotechnology is a raising favorite in popular research segments, particularly with respect to bio-medical applications. Targeted drug treatments have been marked as good opportunity for metal NPs specially SNPs [74]. Their potential has also been identified in the areas of time-release and targeted medications. For instance, a powerful dose of drug can be engineered to be delivered to a particular area while also controlling the release over a specific duration to maximize the effectiveness and ensure patient safety. Since, the absorbed energy from light is radiated into the vicinity of these particles resulting in an increased temperature in their surroundings, making the strong light absorbing SNPs formidable heat mediating objects the application of this characteristic is quite potent as it can be utilized to open polymer micro capsules and good potentially eliminate the cancerous cells as well. It is theorized that these nanoparticles if functionalized with the anti-body designed to target the cancerous cells can be quite effective. Such functionalized NPs particularly bind with the targeted cells which are then destroyed by hyper-thermal therapy through heating the particle ordered tissue. Yet the grey area that remains for such in vivo applications is the probable cytotoxicity of the nanoparticles is a potential danger and must undergo careful investigations. Since, Ag has been found to be non-poisonous and

bio-compatible they do find huge utilization in the elimination of malignant cancerous cells these days [75].

Conclusion

Metal NPs especially silver (Ag) have generated a lot of interest in multiple areas such as nanotechnology, electronics, catalysis, optics, biotechnology, textile engineering, water treatment and bio-medicine. By adjusting the conditions of reaction such as stabilizer, reducing agent and also employing various synthetic methods we can regulate the size, shape and size distribution of SNPs. It is therefore quite important to explain the effects of the condition of reaction on the size of NPs and their morphology as well. Other important parameters in the evaluation of NPs synthesis include particle shape and size and mono dispersity. Hence, it is suggested that efficient regulation on the morphology and mono dispersity of these particles must be researched. The goal being to optimization of reaction conditions. Thus we have seen that there are synthesis techniques that can produce well characterized NPs faster than physical or chemical approaches. These environmental friendly techniques can potentially be utilized in a wide variety of areas including cosmetics, pharmaceuticals, medical applications and foods.

Conflict of interest

The authors declare that there is no conflict of interest.

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