

Anticancer Potential of Biosynthesized Silver Nanoparticles: A Review

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ABSTRACT

The field of nanotechnology has emerged as a promising course of study branching out into various biomedical fields such as therapeutics, imaging, and diagnostics. Metallic nanoparticles, specifically silver, are an important area of study due to their multifunctionality and diverse morphological characteristics. Amongst the various methods of synthesis of these multifunctional nanoparticles such as physical methods and chemical, green synthesis is the most suitable method due to its eco-friendly nature, cost-effectiveness, and ease of production. This article summarizes the broad spectrum of applications of green silver nanoparticles in the fields of cancer theranostics, imaging and diagnosis, and drug delivery. Bimetallic nanoparticles with silver as one of its major constituents are also explored to get a clear insight into the numerous prospective developments in the respective field.

Keywords: Anticancer, biosynthesized, eco-friendly, silver nanoparticles, therapeutic.

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I. INTRODUCTION

Application of nanoparticles in the field of medicine (e.g., antimicrobials (Maria *et al.*, 2015), biosensing (Varghese *et al.*, 2020), imaging (Mukherjee *et al.*, 2014), bioremediation (Salvadori *et al.*, 2022), cosmetics (Gajbhiye and Sakharwade, 2016), among others) has risen exponentially in the last two decades. Nanoparticles are particles whose size ranges from 1-100 nm (Tiquia-Arashiro and Rodrigues, 2016). They have emerged as a very important aspect of modern medicine, as their applications range from imaging to carriers for gene delivery in individual target cells (Annu *et al.*, 2018). Several nanoparticles have multifunctional characteristics such as iron oxide nanoparticles, which are useful in intrinsic imaging as well as in drug delivery (Sharma *et al.*, 2016; Kang *et al.*, 2015).

Theranostics, a novel integration of 'diagnosis' and 'therapeutics' is emerging as a safe, targeted, and efficient pharmacotherapy that focuses on patient-centred care. The term 'Theranostics' was coined by John Funkhouser. It is a new field of medicine that delivers a transition from conventional medicinal practices to the contemporary personalized and precision medicine approach. Theranostics

deals with a specially tailored treatment plan based on the uniqueness of each individual and hence, aids in the prescription of the right drug and treatment protocol for patients under investigation yielding a cost-effective and efficient treatment approach (Jeelani *et al.*, 2014).

To incorporate the versatile benefits of nanoparticles in theranostics, 'theranostic nanoparticles' were developed. These 'theranostic nanoparticles' have a wide range of applications in the diagnostic arena that includes optical imaging, magnetic resonance imaging (MRI), ultrasound, computed tomography, and nuclear imaging (single-photon computed tomography and positron emission tomography) (Zavaleta *et al.*, 2018). Current nanoparticle technologies in the therapy area include drug delivery in cancer patients by liposome-based nanomaterials, neurodegenerative disease therapy, HIV/AIDS therapy, ocular disease therapy, and respiratory disease therapy (Annu *et al.*, 2018). In an ideal scenario, such theranostic nanoparticles should accumulate rapidly and particularly in targeted tissues, efficiently carry out drug delivery without damaging other organs and clear out from the body after a suitable period as nontoxic by-products. This trend of combining therapy and diagnostics is leading to greatly improved personalized disease

management (Abel *et al.*, 2015). The process can be optimized by building more compatible and elaborately designed nanosystems to improve targeting strategies. Theranostics that utilize particles at the nanoscale level have been devised to fabricate a single agent that is a combination of two radioactive drugs; one used for diagnosing the disease and the other used for delivering specialized target therapy to initiate treatment (Zavaleta *et al.*, 2018).

Various types of nanoparticles including gold, platinum, iron, and iron oxides amongst many others have been recognized for their role in different biomedical functions. The rapid and broad range development and the improved practical potential of metallic nanoparticles specifically, has made them an excellent choice in therapeutics, especially in the field of diagnosis, imaging, among others (Azizi *et al.*, 2017). Bio-synthesized silver nanoparticles (b-AgNPs) have been the focal point of several research studies due to their display of versatility and multifunctional biological activities (Mukherjee *et al.*, 2014). Silver nanoparticles exhibit an optical effect that depends on the shape and size of the nanoparticles called localized surface plasmon resonance (LSPR) which enables them to have a range of applications (Abel *et al.*, 2017; Kelly and Johnston, 2014). Silver nanoparticles of small sizes have a very large surface area to volume ratio that allows the attachment and coordination of a large number of ligands, making them a suitable catalyst (Cassano *et al.*, 2018). b-AgNPs exhibit enhanced antibacterial and anti-cancer activities towards cancer cells like human lung cancer cell lines, mouse melanoma cell lines, and human breast cancer cell lines among others. These nanoparticles also exhibit biocompatibility towards multiple human cells making them a suitable drug delivery vehicle. b-AgNPs have been shown to display a unique bright red fluorescence that aids in the process of diagnosis and imaging by detecting the localization of drugs in oncogenic cells and tumor cells (Mukherjee *et al.*, 2014). Along with their biomedical versatility, silver nanoparticles are also more economical than gold nanoparticles, as the cost of production is low and accessibility is more. Biosynthesis of nanoparticles involves using novel methods that are non-hazardous to the environment and further reduces the production costs (Parveen *et al.*, 2016). The current review aims to provide comprehensive detail about green synthesized silver nanoparticles and their potential application as theranostic nanoparticles.

II. GREEN SYNTHESIS OF SILVER NANOPARTICLES AND THEIR THERAPEUTIC APPLICATIONS

Nanoparticles are commonly synthesized using three methods *viz.* (i) Physical method (ii) Chemical method and (iii) Biological method. Chemical methods of nanoparticle synthesis involve using organic and inorganic reducing agents. Physical methods involve techniques like evaporation-condensation and laser ablation for synthesizing nanoparticles. This method has been proven to be beneficial over chemical methods due to the synthesis of uniformly distributed nanoparticles and comparatively less incidence of contamination and environmental pollution as non-toxic solvents are involved (Iravani *et al.*, 2014). Although

physical and chemical methods are easier to perform, these methods pose a threat to the environment due to the extensive use of toxic chemicals as reducing and stabilizing reagents that are non-biodegradable (Vanaja *et al.*, 2014). On the other hand, the biological method or green synthesis of nanoparticles uses biological sources as reducing and capping agents. This method exhibits less toxicity and high efficacy (Nethi *et al.*, 2020). Thus, green synthesis is considered to be an attractive approach due to its ease of production, affordability, and eco-friendly nature (Vanaja *et al.*, 2014). This approach utilizes organisms like bacteria, fungi, and plants as a source of reducing agents for synthesizing different metallic nanoparticles such as gold, silver, cadmium, magnetite, copper, lead, palladium, zinc oxide nanoparticles among others (Iravani *et al.*, 2014; Bilal *et al.*, 2017). Among the different biological methods, plant extracts are considered to be a more viable option due to their ease of maintenance, biosafety, high availability, and cost-effectiveness (Parveen *et al.*, 2016; Kadam *et al.*, 2020).

Plant-mediated green synthesis of nanoparticles is a green chemistry approach that unites the concept of nanotechnology with phytochemistry (Parveen *et al.*, 2016). Additionally, the vast availability of plants facilitates the large-scale production of plant extracts which serve as the reducing agent in nanoparticle synthesis. Plant extracts contain polyphenols and protein constituents which are known to have reducing properties. This ensures the least usage of hazardous chemical reducing agents, thereby reducing the level of toxicity involved in synthesizing such nanoparticles (Mukherjee and Patra, 2017). One of the earliest approaches of plant-based synthesis of silver nanoparticles was with Alfalfa sprouts, owing to their ability to absorb Ag from the agar medium and subsequently transfer it to the shoot region of the plant without any change in the oxidation state. Once reaching the shoot region, these Ag atoms would arrange themselves into nanoparticles by uniting in bundles and forming larger constituents (Gardea-Torresdey *et al.*, 2003; Rauwel *et al.*, 2015). Mukherjee *et al.* (2014) showed that silver nanoparticles could be synthesized from *Oxalis scandens* in a single-step process. These b-AgNPs exhibited not only theranostic ability towards cancer cells but also showed antibacterial properties and fluorescence facilitated imaging. *Seriphidium quettense* along with varying concentrations of AgNO₃ was utilized for the green synthesis of silver nanoparticles (Sq-AgNPs) which were then evaluated for their anti-bacterial, anti-cancer, anti-fungal as well as biocompatibility. The Sq-AgNPs exhibited anti-bacterial activity towards a wide range of bacteria including *Escherichia coli*, *Klebsiella pneumonia*, and *Bacillus subtilis*. Sq-AgNPs also proved to be highly efficacious in prohibiting the proliferation of human liver cancer cells. The results of the hemolytic assay revealed that these nanoparticles were highly biocompatible even at high concentrations making them ideal drug delivery agents (Oasim *et al.*, 2019). b-AgNPs synthesized from the leaf extract of *Butea monosperma* showed anti-proliferative activity towards cancer cells like B16F10, MCF-7 and were found to be biocompatible with the normal cells (Patra *et al.*, 2015). *Zizyphus xylopyrus* bark extract was used to

synthesize silver nanoparticles that could be used as efficient drug delivery systems due to their biocompatibility with the host cells (Maria *et al.*, 2015). The mycelia extract of fungal precursors such as *Ganoderma neo-japonicum* was also employed for the synthesis of silver nanoparticles to target the cell viability and membrane leakage system of human breast cancer cells. The consecutive treatment of MDA-MB-231 breast cancer cells with varying concentrations of b-AgNPs revealed that the cell viability of the cancer cells was prohibited and cell damage was observed due to membrane leakage induced by these AgNPs (Gurunathan *et al.*, 2013). M. J. Ahmed *et al.* (2019), tested the therapeutic potential of the plant *Jurinea dolomiaea* against cervical cancer cell lines (HeLa) and breast cancer cell lines (MCF-7). This *in-vitro* study of cytotoxic properties of silver nanoparticles synthesized from the leaf extract of *J. dolomiaea* not only proved its anti-cancer potential but also the antioxidant properties possessed by the plant. The apoptosis study also proved the high biocompatibility levels of these b-AgNPs as compared to Cisplatin, a common chemotherapeutic drug (Ahmed *et al.*, 2019). The anti-cancer potential and apoptotic activity of silver theranostic nanoparticles synthesized using *Fagonia indica* against human breast cancer cells were studied by Ullah *et al.* (2020). Different mechanistic assays like Acridine orange/Ethidium Bromide (AO/EB) assay, DAPI assay, and Annexin V/PI assay were used to study and unveil the mechanism of action of these b-AgNPs. It was found that the b-AgNPs triggered the activation of caspases 3 and 9, which caused morphological changes in the plasma membrane of the cancer cells, leading to nuclear condensation followed by apoptosis (Ullah *et al.*, 2020). The wide variety of plants used for the green synthesis of silver nanoparticles exhibits the vast and unexplored potential of these silver nanoparticles in the area of theranostics.

The anti-diabetic and cardioprotective potential of silver nanoparticles synthesized from the plant *Syzygium cumini* were tested by Atale *et al.* (2017). The results of this study concluded that *S. cumini* derived silver nanoparticles were efficacious in suppressing glucose-induced cardiac stress. The mechanism of action was found to be the maintenance of the cellular integrity and reduction in the oxidative stress (Atale *et al.*, 2017).

Zeedan *et al.* (2020), conducted an *in-vivo* and *in-vitro* experiment to test the anti-viral effects of silver nanoparticles synthesized from olive leaves and natural honey. The antiviral efficacy was tested using MDBK cell culture and experimental animals. These green AgNPs were found to protect the MDBK cell culture and the experimental animals from the BoHV-1 (bovine alpha herpesvirus 1) proving their antiviral potential. b-AgNPs synthesized from *Oscillatoria sp.* and *Spirulina platensis* were checked for their antiviral property and were found to be highly effective against the Herpes Simplex virus (El-Sheekh *et al.*, 2020).

III. APPLICATIONS OF GREEN SYNTHESIZED SILVER NANOPARTICLES IN CANCER THERAPY

According to a WHO report in 2018, cancer is one of the leading causes of death worldwide (Aziz *et al.*, 2019).

Cancer therapy mostly includes surgery, chemotherapy, and radiation therapy and is widely known to have harsh side effects such as increased toxicity, damage of healthy cells, and tumor recurrence (Cherukula *et al.*, 2016). Three of the most common cancers include lung cancer, breast cancer, and colon cancer, of which lung cancer has the highest fatality rate. The primary cause of cancer is uncontrolled cell growth and proliferation induced due to variations in gene expression and subsequent metastasis of the tumor cells to distant tissues and organs (Aziz *et al.*, 2019; Balakumaran *et al.*, 2015). The urgent need for specialized, targeted therapy arises as a result of long-term adverse effects induced by anti-cancer drugs in the systemic circulation and poor prognosis of such treatment procedures (Yhee *et al.*, 2014).

The use of biosynthesized silver theranostic nanoparticles for cancer therapy can prove to be an effective, alternative approach to the conventional methods used for cancer treatment (Cherukula *et al.*, 2016). Nanoparticles possess immense potential in specialized cancer therapy due to their unique physical, chemical, and biomedical properties which, as mentioned earlier, are attributed to their small size, large surface area, and diverse pharmacological properties, for instance, biocompatibility, cancer-killing ability, as imaging facilitators among others (Yhee *et al.*, 2014). Biosynthesized silver theranostic nanoparticles have gained attention due to their role in cancer diagnosis and alternative targeted drug delivery systems (Karmous *et al.*, 2020; Madamsetty *et al.*, 2019). These nanoparticles either damage tumor cells and oncogenes or protect healthy cells from cancerous cells using mechanisms that employ the antioxidative and antitumor properties found in plants (Karmous *et al.*, 2020). The mechanism of action differs in different b-AgNPs based on their plant precursors. This mechanism ranges from cell cycle arrest, inhibition of angiogenesis, membrane damage, and leakage, DNA damage, mitochondrial destruction, misfolding of proteins, apoptotic cell death, among others (Aziz *et al.*, 2019; Gurunathan *et al.*, 2013; Mukherjee *et al.*, 2014; Patra *et al.*, 2015; Ullah *et al.*, 2020; Liang *et al.*, 2015; Kuppusamy *et al.*, 2016). The choice of plant species, type of extract, and concentration of phytochemicals are of prime importance during the synthesis of nanoparticles. A rise in metal concentration or leaching of trace elements from biosynthesized metal nanoparticles can cause an increase in oxidative stress which can, in turn, increase the risk of cancer (Karmous *et al.*, 2020).

A. Role of b-AgNPs as theranostics in Breast Cancer Therapy

Breast cancer, a type of adenocarcinoma, is the second most commonly occurring cancer in the world and also a major cause of cancer deaths among women (Gurunathan *et al.*, 2013; Jemal *et al.*, 2002). MDA-MB-231 and MCF-7 are two of the most commonly studied human breast cancer cell lines (Gurunathan *et al.*, 2013).

Silver nanoparticles have been shown to display promising results in inhibiting cell growth of breast cancer cells *in-vitro*. S. Dinparvar *et al.* (2020), b-AgNPs from the seed extract of the plant *Cuminum cyminum* and checked its efficacy against human breast cancer cell line MCF-7 and human breast metastatic cancer cell line AU565. The action of chemically synthesized AgNPs and b-AgNPs was

compared by a cytotoxic analysis and an anticancer study. b-AgNPs were not only non-toxic but also exhibited strong inhibitory effects against human breast cancer cell lines at 0.25 and 0.5 µg/ml. Both b-AgNPs and chemically synthesized AgNPs showed strong inhibition against cancer cells, but b-AgNPs proved to be far less cytotoxic than the latter (Dinparvar *et al.*, 2020). Jeyaraj *et al.* (2013) used *Sesbania grandiflora* leaf extract as a substitute for a reducing agent while biosynthesizing AgNPs to check their inhibitory action against human breast cancer cell line MCF-7. MTT, AOEB, Hoechst, and COMET assays proved the effective anti-proliferative effect of these b-AgNPs against MCF-7. Cell damage was induced by multiple pathways including membrane damage, increase in oxidative stress, and apoptosis (Jeyaraj *et al.*, 2013). In a similar study conducted by Ramar *et al.* (2015), *Solanum trilobatum* was used to synthesize silver nanoparticles and tested for *in-vitro* anticancer effect on MCF-7 cell line and was proven to be extremely effective (Ramar *et al.*, 2015). Cytotoxicity studies conducted on b-AgNPs synthesized from the root extract of *Rheum emodi* also showed their anti-cancer activity against MCF-7 in a dose-dependent manner (Sharma *et al.*, 2015). Heydari and Rashidipour (2015), used the extract of Oak fruit hull for the preparation of silver nanoparticles and tested their cytotoxicity against MCF-7 cell line. Silver nanoparticles synthesized from *Melia dubia* leaf extract by Kathiravan *et al.* (2014), showed phenomenal anticancer activity against human breast cancer cell line KB. *Piper longum* fruit used by Reddy *et al.* (2014), to prepare b-AgNPs showed strong anti-cancer activity against the MCF-7 cell line. b-AgNPs synthesized from the aqueous extract of *Citrullus colocynthis* showed active anti-cancer activity against multiple cancer cell lines including MCF-7 (Shawkey *et al.*, 2013).

Analysis of cytotoxicity of b-AgNPs synthesized from *Fagonia indica* was conducted using the MTT cell viability assay (3-(4,5-Dimethylthiazol-2-Y1)-2,5-diphenyltetrazolium bromide). The results displayed that the inhibition in the growth of *in-vitro* cultured breast cancer cells was influenced by the concentration of b-AgNPs. Alteration in nuclear chromatin morphology and apoptosis were studied using the DAPI assay and Annexin V/PI flow cytometric assay. The results showed that the nanoparticle-treated cells had a distinct bright colour, abnormal nuclei, and condensed chromatin with irregular cell structure (Ullah *et al.*, 2020). These results were in accordance with previous research work on the influence of green synthesized theranostic nanoparticles on MCF-7 cell lines (Venugopal and Rather *et al.*, 2017; Bhattacharyya *et al.*, 2008; Kathivaran *et al.*, 2014). The AO/EB assay exhibited the mechanism of action of membrane damage of the MCF-7 cells (Ullah *et al.*, 2020; Venugopal *et al.*, 2017). The b-AgNPs treated cells showed shrinkage, membrane blebbing, and nuclear fragmentation leading to cell damage and subsequent apoptosis (Ullah *et al.*, 2020; Patra *et al.*, 2015). Annexin V/Propidium Iodide apoptosis detection assay conducted by several researchers indicated the possibility of inducible apoptosis via autophagy, mitochondrial dysfunction, lipid peroxidation and arresting of the cell cycle (Ullah *et al.*, 2020; Liang *et al.*, 2015; Venugopal *et al.*, 2017; Kikuchi *et al.*, 2012). Previous studies have

shown that b-AgNPs inactivate caspases which are known to be involved in apoptosis and sometimes cause inflammation (Mukherjee *et al.*, 2014). The formation of reactive oxygen species (ROS) induces oxidative stress on the cell which causes malfunction of various cell components, cell cycle as well as DNA damage, endoplasmic reticulum stress conditions, and misfolding of proteins (Mukherjee *et al.*, 2014; Ullah *et al.*, 2020; Kikuchi *et al.*, 2012; Azizi *et al.*, 2017). All the results indicate a positive response towards green synthesized silver nanoparticle therapy against breast cancer cells and a definitive need for further research and development in this field.

B. Role of b-AgNPs as theranostics in Lung Cancer Therapy

Lung cancer, another type of adenocarcinoma, prevails to be a major public health hazard and the most fatal cancer-causing maximum deaths worldwide (Barabadi *et al.*, 2020). Lung cancer screening and diagnosis are usually done with a computerized tomography (CT) scan. Venkatesan *et al.* (2014) biosynthesized silver nanoparticles from *Rosa damascena* and checked their efficacy against human lung cancer cell line A549. These nanoparticles were not only hemocompatible but also exhibited anti-cancer activity against human lung cancer, although the mechanism is unclear (Venkatesan *et al.*, 2014). Another study conducted by Khanra *et al.* (2015), involved the biosynthesis of silver nanoparticles using the leaf extract of *Scoparia dulcis* and checking its anti-proliferative efficacy against the A549 cell line. Along with having high antimicrobial activity *S. dulcis* also showed anti-cancer activity against A549 and PA-1 (human ovary cell line) making it a promising therapeutic agent in the future (Khanra *et al.*, 2015). b-AgNPs synthesized from a seagrass *Cymodocea serrulata* also showed high cytotoxic potential and anticancer activity against A549, making it a candidate as a non-toxic cancer therapy agent (Palanippa *et al.*, 2015). Khanra *et al.* (2016), used *Croton bonplandianum* Baill. leaves to prepare AgNPs and evaluate their anti-cancer activity against A549. The MTT assay revealed the strong anti-cancer potential of b-AgNPs and, it was found that the nanoparticles acted by reducing ATP content due to mitochondrial damage. This further increased the production of ROS species leading to a rise in oxidative stress (Khanra *et al.*, 2016). b-AgNPs prepared from *Ola scandens* also exhibited enhanced anti-cancer activity against the A549 cell line (Mukherjee *et al.*, 2014). One of the notable studies on *in-vitro* and *in-vivo* applications of b-AgNPs against lung cancer showed that AgNPs significantly suppressed proliferation of H1299 lung cancer cell lines and tumor growth in xenograft severe combined immunodeficient mouse model. Further, the AgNPs also induced apoptosis in a dose-dependent manner by increasing caspase 3 and surviving levels (He *et al.*, 2016). Silver nanoparticles extracted from *Punica granatum* exhibited strong anti-cancer activity by cell growth inhibition of the A549 cells (Annu *et al.*, 2018). MTT cell viability assay conducted by various researchers in diverse projects confirmed no cytotoxic effects on normal cell growth and non-proliferative nature for cancerous cells (Annu *et al.*, 2018; Mukherjee *et al.*, 2014; Venugopal *et al.*, 2017). b-AgNPs have different mechanisms of action that enable them to curb the growth of cancerous cells, one of

them being creating oxidative stress and activation of apoptosis pathway by upregulation of the p53 protein (Mukherjee *et al.*, 2014; Mei *et al.*, 2012; Gurunathan *et al.*, 2013; Fridman and Lowe, 2003). DNA damage in A549 cells was also a frequently observed side effect caused due to interruption of the mitochondrial respiratory chain as well as arresting the cell cycle at the G2/M phase (Mukherjee *et al.*, 2014; Annu *et al.*, 2018). Oxidative stress was generated by using H₂O₂ which helped in measuring the intracellular ROS scavenging that led to the malfunctioning of cellular organelles (Annu *et al.*, 2018). It can be easily concluded that b-AgNPs have huge unexplored potential in the field of lung cancer theranostics.

C. Role of b-AgNPs as theranostics in Colon Cancer Therapy

Colon cancer is the third most common cancer worldwide. Almost 10% of cancer deaths are caused by colon cancer and the diagnosis is confirmed by colonoscopy, stool DNA test, Sigmoidoscopy, or Guaiac based fecal occult blood test. P. Kuppusamy *et al.* (2016), made use of an aqueous extract of *Commelina nudiflora* to synthesize AgNPs and study their anti-colon cancer properties. The b-AgNPs exhibited reduced cell viability coupled with increased cell cytotoxicity in HCT-116 colon cancer cells. In the same study, the mRNA gene expression in the HCT-116 cells was analyzed. Interestingly, it was observed that the expression of pro-apoptotic genes coding for Caspase 3, Caspase 8, and Caspase 9 was more upregulated in HCT-116 cell lines that were treated with the b-AgNPs as compared to those treated with a normal chemotherapeutic drug, Cisplatin (Kuppusamy *et al.*, 2016).

b-AgNPs synthesized from *Pimpinella anisum* seeds have also showed high cytotoxicity and reduced cell viability in HT115 colon cancers (AlSalhi *et al.*, 2016). Anti-cancer activity of *Rosa indica* was analyzed against HCT15 colon cancer cells, and was found to be a good anti-cancer agent as it reduced cancer cell viability, Bcl-2 expression, increased Bax levels, and caspase 3 and caspase 9 activities that induce apoptosis (Manikandan *et al.*, 2015). Another study utilized leaf extract of *Vitex negundo* for synthesizing AgNPs and studied their efficacy against HCT15. The results of the MTT cell viability showed strong inhibition of cancer cell proliferation. The nuclear morphology study using propidium iodide staining showed an increase in apoptosis and cell cycle arrest at G0/G1 and G2/M phases (Prabhu *et al.*, 2013). *Gymnema sylvestre* was used by Arunachalam *et al.* (2015), to prepare b-AgNPs to study and analyze their potential anticancer activity against HT29 human colon cancer cell line. They found that once the nanoparticles penetrated the cell by various mechanisms like phagocytosis, pinocytosis, and endocytosis, DNA damage and apoptosis (Arunachalam *et al.*, 2015). All these findings point towards the promising applications of green synthesized silver theranostic nanoparticles in combating cancer.

D. Role of b-AgNPs as theranostics in other forms of cancer

Biosynthesized theranostic AgNPs prepared from a wide variety of plants are also being studied for their role in cancer therapies for many different types of less common

cancers. Jeyaraj *et al.* (2013), used b-AgNPs synthesized from *Podophyllum hexandrum* to check its cytotoxic efficacy and to study the role of caspases in apoptosis on the human cervical cancer cell line, HeLa. It was found that these nanoparticles could selectively target and inhibit the cell cycle and mechanism of HeLa cells by inducing DNA damage and caspase-induced cell death (Jeyaraj *et al.* 2013). *Heliotropium indicum* was used to synthesize silver nanoparticles whose anti-cancer efficacy was checked against HeLa cancerous cells. Results of the MTT assay revealed that these b-AgNPs successfully inhibited the growth of HeLa cells in a dose and time-dependent manner. Their anti-cancer activity was attributed to their amphiphilic and membrane penetrative nature as well as their ability to induce a state of hypoxia in the cells (Vijjstella, 2014). Sukirtha *et al.* (2012), used *Melia azedarach* to synthesize b-AgNPs for an *in-vitro* study of their effect on HeLa cancer cells. The anti-cancer activity of the nanoparticles was found to be in a dose-dependent manner with a lethal dose value of 300µg/ml against the HeLa cell line (Sukirtha *et al.*, 2012). Mishra *et al.* (2012), studied the anti-cancer effect of *Azadirachta indica* b-AgNPs on the SiHa cervical cancer cell line. They reported the vast anti-cancer potential of *A. indica* along with it being a very cost-effective anti-cancer therapeutic agent as well.

Detailed study of laryngeal cancer therapy was also done by researchers. Devi and Bhimba (2012), used the seaweed *Ulva lactuca* to biosynthesize silver nanoparticles and test their anticancer efficacy against Hep-2 laryngeal cancer cell line. The potential anti-proliferative effect of b-AgNPs against Hep-2 cells was confirmed and was found to be nontoxic to the normal cells (Ahmad *et al.*, 2010). The biomedical potential of the plant *Citrullus colocynthis* was tested against Hep-2 cell line by Satyavani *et al.* (2011). These b-AgNPs inhibited the growth of the cancerous cells in a dosage-dependent manner by DNA damage followed by apoptosis (Satyavani *et al.*, 2011). Another very important study involved the use of *Suaeda monoica* leaf extract to prepare b-AgNPs and testing their anti-cancer potential against Hep-2 cancer cells. A partial reduction in the viability of the cancer cells was induced at a lethal dose value of 500nM. This anti-cancer potential was attributed to the intracellular physicochemical interaction of the b-AgNPs with the proteins and phosphate groups as well as the nitrogen bases in the DNA (Satyavani *et al.*, 2012).

Andean mora leaf was used to biosynthesize silver nanoparticles and its anti-proliferative effect on Hep-G2 human liver cancer cells was checked. This study paved the way for the effective use of b-AgNPs in not only anti-cancer therapy but also drug delivery (Kumar *et al.*, 2016). Studies conducted on the anti-cancer activity of *Allium sativum* b-AgNPs against Hep-G2 cancer cells found potential cell inhibitory effects against the cancer cells making it a valuable anti-cancer drug in the future (Pandian *et al.*, 2015). Silver nanoparticles biosynthesized using the root extract of *Citrullus colocynthis* by Shawkey *et al.* (2013), were used to reveal its anti-cancer activity against multiple cancer types including breast cancer, colon cancer, liver cancer and intestine cancer. All these results prove the extremely vast potential of b-AgNPs in the arena of cancer

theranostics due to their non-toxic, cost-effective and easily penetrative nature.

IV. APPLICATION OF B-AGNPS IN IMAGING AND DIAGNOSIS

The versatile nature of green theranostic nanoparticles allows them to be used for a wide range of biomedical applications like diagnostic screening, fluorescence imaging, drug delivery, etc. The multifunctional properties possessed by biologically synthesized nanoparticles assist in providing multiple imaging platforms for easy and rapid disease verification and exact localization of tumor cells and damaged tissues. The individual properties of these multifunctional nanoparticles are harboured by altering the surface properties to match the required application (Ahmed *et al.*, 2012).

Plant extracted organic dye molecules are now being studied and applied for thermal imaging due to their low tissue absorbance and enhanced photothermal effects (Cherukula *et al.*, 2016). The various phytochemicals present in plants and their penetrative nature are now being exploited for their fluorescence abilities. The fluorescent molecules present inside the plant cell complex with b-AgNPs, penetrate the cells when incubated with such b-AgNPs. These b-AgNPs with fluorescent properties can facilitate early diagnostic screening of serious diseases such as cancer. This principle was studied by performing fluorescence imaging of A549 human lung cancer and B16 mouse melanoma cell lines after treating them with b-AgNPs treated with the extract of *Ola scandens*. The cell lines treated with b-AgNPs displayed red fluorescence which was also the characteristic fluorescence displayed by the phytochemicals present in the *Ola* extract. Surprisingly, chemically synthesized AgNPs did not display any peculiar red fluorescence (Mukherjee *et al.*, 2014).

He *et al.* (2013), successfully synthesized b-AgNPs from the extract of *Chrysanthemum morifolium* and explored the biomedical application of these nanoparticles in clinical ultrasound gel for diagnosis. Diagnosis of a specific ailment using nanoparticles in molecular imaging involves analyzing the correlation of the signal generated with the phenotype. The size of the diseased area, along with the cancer stage and biochemical nature can be analyzed using the location and intensity of nanoparticle signals generated at the target site. An ideal nanoparticle system should possess a central imaging core surrounded by small molecule therapeutic agents. The presence of a cloak of protective polymer can protect these nanoparticle systems from immune cells and, the system, in turn, uses ligands such as IgG for active targeting. Most clinically viable silver nanoparticles are used in magnetic resonance screening while the other types are being modified in terms of their toxicity and biodistribution profiles to enhance their biocompatibility (Jokerst and Gambhir, 2011).

Theranostic nanoparticles and their applications in biomedical fields and cancer theranostics have been ongoing for the past several years, but many challenges remain. One of the major challenges is the formulation of nanoparticles with multi functionalities making the nano-system extremely complicated. To ensure successful application of theranostics nanomedicine, appropriate imaging choice must

be made, and considerable *in-vivo* assessment is highly required (Madamsetty *et al.*, 2019). Although limited research has been performed in the application of green synthesized silver theranostic nanoparticles in imaging and diagnosis, extensive clinical research is still required to unearth its vast undiscovered potential and scope in the future.

V. APPLICATIONS OF GREEN SYNTHESIZED SILVER NANOPARTICLES IN DRUG DELIVERY

Nanoparticle-based drug delivery systems and vehicles (such as nano metal particles, polymers, and biological materials) have been extensively studied due to their diagnostic and theranostic properties (Mukherjee *et al.*, 2014; Ahmad *et al.*, 2010; Jahangiran *et al.*, 2017). Currently, cancer is the most common and widely studied and evaluated disease for nano vehicle-based targeted delivery, followed by neurodegenerative diseases, certain infections, and autoimmune diseases (Yetisgin *et al.*, 2020). The demand for such an efficacious system has increased due to the reduced circulation time and limited target efficiency of the currently available treatments (Xie *et al.*, 2017). An ideal, efficient targeted delivery system includes the vehicle loaded with the drug or delivery agent being retained in the circulatory system of the organism's body for a desirable amount of time, protecting themselves from the immune system of the body, and lastly releasing the drug at the target site (Yetisgin *et al.*, 2020). Nano-vehicles protect the externally injected chemotherapeutic agents, genes, and imaging agents against the harsh environment in systemic circulation ensuring targeted delivery (Xie *et al.*, 2017). However, it should be noted that such systems need to be experimentally analyzed first for their safety before using them in an *in-vivo* model, specifically animal models (Mukherjee *et al.*, 2014). Due to their small size and penetrative nature, nanoparticles can easily enter the human body, much faster than larger-sized commercial drugs. Furthermore, the use of biosynthesized nanoparticles for drug delivery poses a lesser risk as compared to the adverse effects caused by toxic pharmaceuticals, as no harmful reducing or capping agents are used (Lam *et al.*, 2017). The nanoparticle-based drug delivery systems can be used for the delivery of nontoxic prodrugs to tumor cells and damaged tissues. Cellular stimulus at the target site or damaged tissue converts this prodrug to a toxic form which causes subsequent and selective damage of tumor cells and damaged tissue (Sahoo *et al.*, 2016).

Mukherjee *et al.* (2014), tested the *in-vivo* biocompatibility of b-AgNPs based nanocarriers towards different types of normal cells including human umbilical vein endothelial cells (HUVEC), rat cardio myoblast cell line (H9C2), and Chinese hamster cell line (CHO), and used the MTT assay to track their metabolic activities. It was found that b-AgNPs were nontoxic to the cells even at a higher concentration as opposed to chemically synthesized AgNPs, thereby indicating their suitability for *in-vivo* applications as drug delivery vehicles or carriers.

In another study, polyethylene glycol-silver (PEGylated) decorated graphene nanocomposites (NGO-AgNPs-PEG) synthesized from *Azadirachta indica* extract were subjected

to a novel syn-graphenization method and studied for their capability as a nano-vehicle for drug delivery against cancer cells. A comparative study assessing the effect of cancer drug, free doxorubicin (DOX) and DOX loaded NGO-AgNPs-PEG on HeLa cancer cells and HaCaT cancer cells were conducted. Based on the drug loading and unloading efficiency study and response to pH stimulus it was seen that the DOX released from the NGO-AgNP-PEGs was 218% more efficient than the free DOX. This proves that these silver nanoparticles could also act as subsidiary carriers or as a supportive driving force for the delivery of the drugs to the selective cells or tissues. The anti-proliferative study on the HaCaT cells showed that the DOX-loaded b-AgNPs were less harmful to normal cells as compared to free DOX. This study elaborates the promising prospects of NGO-AgNP-PEGs in targeted and controlled drug delivery therapies (Palai *et al.*, 2019).

Nano-based targeted delivery systems in infectious disease therapy are mostly used for antimicrobial drugs (Sahoo *et al.*, 2016). Metallic nanoparticles, specifically silver nanoparticles have been used for the *in-vitro* evaluation of *Candida albicans* and *Escherichia coli* with the conjugated drugs being Fluconazole (FLC) and Ampicillin respectively (Yetisgin *et al.*, 2020; Longhi *et al.*, 2015; Brown *et al.*, 2012). Longhi *et al.* (2015), studied the antifungal effect of silver nanoparticles biosynthesized from *Fusarium oxysporum* individually and then paired with the antifungal drug FLC. The effect of the b-AgNPs alone was almost negligible but in combination with FLC, the growth of *C. albicans* was reduced by 16 to 64 times. A dose-dependent decrease was observed in the cell viability of the biofilm proving that b-AgNPs could be used as an effective control agent against microbial diseases causing infection (Longhi *et al.*, 2015).

Optimization of the drug encapsulation process and high duplicability at considerably lower cost are important factors that impact the amalgamation of theranostic nanomedicine in the clinical field (Madamsetty *et al.*, 2019). Green synthesized nanomaterials are also being studied in the field of gel dosimetry for radiotherapy, but there is still a broad field of study yet to be unraveled and explored (Vedelago *et al.*, 2018). In recent years, much encouraging evidence has sprouted that ensures a positive outlook for bio-inspired and green synthesized theranostic nanoparticles and their clinical applications in not an only cancer treatment, but a wide range of biomedical applications (Madamsetty *et al.*, 2019).

VI. BIMETALLIC NANOPARTICLES AND THEIR APPLICATIONS

Bimetallic nanoparticles have been gaining recognition and scientific attention for their multifunctionality and superior properties over monometallic nanoparticles. The knowledge and information available about biomedical applications of bimetallic nanoparticles, specifically green synthesized bimetallic nanoparticles, is scarce because of limited research and experimentation being conducted in this respective arena. Despite their ease of production, cost-effectiveness and eco-friendly nature, the mechanisms of synthesis of these nanoparticles have been poorly explored (Duran and Seabra, 2018).

The introduction of a second metal for the formation of a heterogeneous bimetallic structure instantly enhances the attractiveness and the therapeutic potential of the resultant structure as useful properties of both metals have a better effect when used in a combination in comparison to when used singly. The addition of a new metal heavily influences the structural and intrinsic properties of the nanoparticles by the enhancement of the magnetic, optical as well as plasmonic properties, while also maintaining stability (Srinoi *et al.*, 2018). Silver (Ag) and gold (Au) nanoparticles have been thoroughly explored by researchers for their wide range of biomedical and theranostic applications including anti-cancer, anti-microbial, anti-fungal, and antioxidant activities. A combination of the two to form bimetallic nanoparticles has been known to have better biocompatibility and unique properties as compared to that arising from both noble metals individually (Gupta *et al.*, 2020). In the case of Ag-Au nanoparticles, the surface plasmon resonance levels can be altered according to the required structural characteristics just by controlling the Ag: Au ratio in the displacement reaction taking place during the synthesis of this bimetallic structure. This flexibility allows the bimetallic structure to have variable shapes and high optical activity (Srinoi *et al.*, 2018). This section will explore green synthesized bimetallic nanoparticles containing silver and their theranostic applications.

Sivamaruthi *et al.* (2019) studied the biosynthesis of silver-palladium (Ag-Pd) nanoparticles from the fruit extract of *Terminalia chebula*. The anti-cancer analysis showed that the nanoparticles acted by inducing the production of ROS which in turn leads to mitochondrial damage and subsequent apoptosis. The antimicrobial study was conducted by checking its effectiveness against the methicillin-resistant bacteria *Staphylococcus aureus* and *Pseudomonas aeruginosa* and was found to be efficacious against both species. The cytotoxic studies also showed that these bimetallic nanoparticles were harmless towards the normal body cells and had no undesirable hemolytic effect as well (Sivamaruthi *et al.*, 2019).

Jiang *et al.* (2019) developed a novel method of synthesis of Ag-Au bimetallic nanoparticles using *Escherichia coli* and studied their various biomedical applications. The Au-Ag nanoparticles were found to have a wide spectrum of applications in various fields including ultrafast colorimetric detection of H₂O₂, photothermal therapy, and antibiotic therapy. Moreover, these nanoparticles were found to have effective anti-bacterial properties without any harmful cytotoxic side effects, guaranteeing the bright future of Ag and Au in the biomedical field (Jiang *et al.*, 2019).

Another interesting study conducted by Lateef *et al.* (2016), used *Cola nitida*, commonly referred to as Kolanut for the biosynthesis of Ag-Au nanoparticles. The antifungal study of these nanoparticles revealed that they were efficacious against *Aspergillus flavus*, *Aspergillus fumigatus*, and *Aspergillus niger*. The Kolanut nanoparticles were also studied for their larvicidal properties and exhibited a mortality rate of 80-100% within 24 hours, when exposed to the Anopheles mosquito larva. These nanoparticles also showed blood anticoagulation properties as well as thrombolytic potential making them suitable for

the management of blood coagulation disorders (Lateef *et al.*, 2016).

Gupta *et al.* (2020), drew a comparative study of the potential anticancer properties of photosynthesized mono and bimetallic nanoparticles. Ag, Au and Ag-Au nanoparticles were synthesized using the aqueous leaf extract of *Moringa oleifera*. The results exhibited the effectiveness of the Ag-Au nanoparticles against the Hep2

cell line (Gupta *et al.*, 2020). Bimetallic nanoparticles are making their way into the diagnostic and therapeutic sciences, thus making them extremely ideal theranostic agents and are also being studied for various biomedical applications that include drug delivery, antimicrobial property, antifungal nature, larvicidal nature amongst others.

TABLE I: ANTICANCER ACTIVITIES OF BIOSYNTHESIZED SILVER NANOPARTICLES

Study	Plant Species	Size of Nanoparticles	Properties exhibited
Maria <i>et al.</i> , 2014	<i>Zizyphus xylopyrus</i>	60-70 nm	Antimicrobial, Drug delivery system
Mukherjee <i>et al.</i> , 2014	<i>Oxalis scandens</i>	30-60 nm	Antibacterial, Anti-cancer on human lung cancer, breast cancer, and mouse melanoma, Drug delivery vehicle, Imaging facilitator
Annu <i>et al.</i> , 2018	<i>Punica granatum</i>	6-45 nm	Anti-cancer towards human lung cancer, Antibacterial, Antioxidant
Kadam <i>et al.</i> , 2020	<i>Brassica oleracea</i> var. <i>botrytis</i>	35.08 nm	Photocatalytic activity for degrading MB dye, Biosensing of Hg ²⁺ ion
Vedelago <i>et al.</i> , 2018	<i>Seriphidium quettense</i>	120.4 nm	Antibacterial, Anti-cancer on human liver cancer, Antifungal, High biocompatibility towards healthy erythrocytes
Gurunathan <i>et al.</i> , 2013	<i>Ganoderma neo-japonicum</i>	5 nm	Cytotoxic effects, Apoptotic features on human breast cancer
Ahmed <i>et al.</i> , 2019	<i>Jurinea dolomiaea</i>	-	Anti-cancer towards human cervical cancer and human breast cancer, Antioxidant potential
Ullah <i>et al.</i> , 2020	<i>Fagonia indica</i>	10-60 nm	Anti-cancer on human breast cancer, Antioxidant, Apoptotic features, Activating caspase 3 and 9
Atale <i>et al.</i> , 2017	<i>Syzygium cumini</i>	40-100 nm	Anti-diabetic, Cardioprotective potential
Aziz <i>et al.</i> , 2019	<i>Piriformospora indica</i>	6-15 nm	Anti-cancer on human breast cancer, liver cancer, and cervical cancer
Balakumaran <i>et al.</i> , 2015	<i>Guignardia mangiferae</i>	5-30 nm	Antibacterial, Anti-cancer activity on human cervical cancer and breast cancer, Antifungal
Venugopal <i>et al.</i> , 2017	<i>Beta vulgaris</i>	5-20 nm	Anti-cancer effect on human breast cancer, lung cancer, and pharynx cancer
Kuppusamy <i>et al.</i> , 2016	<i>Commelina nudiflora</i>	24-150 nm	Anti-cancer effect on human colon cancer
Dinparvar <i>et al.</i> , 2020	<i>Cuminum cyminum</i>	-	Anti-cancer on human breast cancer
Jeyaraj <i>et al.</i> , 2013	<i>Sesbania grandiflora</i>	22 nm	Anti-cancer on human breast cancer
Ramar <i>et al.</i> , 2015	<i>Solanum trilobatum</i>	41.90 nm	Antibacterial, Anticancer on human breast cancer
Sharma <i>et al.</i> , 2015	<i>Rheum emodi</i>	27.50 nm	Anti-cancer on human breast cancer
Heydari <i>et al.</i> , 2015	<i>Oak fruit hull</i>	40 nm	Anti-cancer on human breast cancer
Kathiravan <i>et al.</i> , 2014	<i>Melia dubia</i>	7.3 nm	Anti-cancer on human breast cancer
Reddy <i>et al.</i> , 2013	<i>Piper longum</i>	46 nm	Antimicrobial, Anti-cancer on human breast cancer, Antioxidant
Shawkey <i>et al.</i> , 2011	<i>Citrullus colocynthis</i>	7-19 nm	Anti-cancer effect on human breast cancer, liver cancer, colon cancer, and intestinal cancer
Venugopal <i>et al.</i> , 2017	<i>Syzygium aromaticum</i>	5-20 nm	Anti-cancer on human breast cancer and lung cancer
Bhattacharya <i>et al.</i> , 2008	<i>Gelsemium sempervirens</i>	-	Anti-cancer effect on human cervical cancer
Venkatesan <i>et al.</i> , 2014	<i>Rosa damascena</i>	84 nm	Anti-cancer potential towards human lung adenocarcinoma, Biocompatibility (selectively destroys cancer cells, while leaving healthy cells untouched)
Khanra <i>et al.</i> , 2015	<i>Scoparia dulcis</i>	15-25 nm	Antibacterial, anti-cancer effect on human lung cancer
Palaniappan <i>et al.</i> , 2014	<i>Cymodocea serrullata</i>	29.28 nm	Anti-cancer effect on human lung cancer
Khanra <i>et al.</i> , 2015	<i>Croton bonplandianum</i>	15-40 nm	Antibacterial, anti-cancer effects on human ovarian cancer and human lung cancer
AlSalhi <i>et al.</i> , 2016	<i>Pimpinella anisum</i>	3.2-16 nm	Antimicrobial, Anti-cancer property towards human neonatal skin cancer and human colon cancer
Manikandan <i>et al.</i> , 2015	<i>Rosa indica</i>	23.52-60.83 nm	Antibacterial, Anti-cancer effect on human colon adenocarcinoma, Anti-inflammatory
Prabhu <i>et al.</i> , 2013	<i>Vitex negundo</i>	22 nm	Anti-cancer effect on human colon cancer, Apoptotic features
Arunachalam <i>et al.</i> , 2014	<i>Gymnema sylvestre</i>	-	Anti-cancer property towards human colon adenocarcinoma, Anti-ulcerative
Jeyaraj <i>et al.</i> , 2012	<i>Podophyllum hexandrum</i>	14 nm	Anti-cancer on human cervical cancer
Vijistella <i>et al.</i> , 2014	<i>Heliotropium indicum</i>	80-90 nm	Anti-cancer effect on human cervical cancer, antimicrobial potency
Sukirtha <i>et al.</i> , 2011	<i>Melia azadarach</i>	78 nm	Anti-cancer property on human cervical cancer and mouse lymphoma
Mishra <i>et al.</i> , 2012	<i>Azadirachta indica</i>	2-18 nm	Anti-cancer on human cervical cancer
Devi <i>et al.</i> , 2012	<i>Ulva lactuca</i>	20-56 nm	Anti-cancer towards human breast cancer, cervical cancer, and intestinal cancer
Satyavani <i>et al.</i> , 2011	<i>Citrullus colocynthis</i>	31 nm	Anti-cancer towards human larynx cancer
Satyavani <i>et al.</i> , 2012	<i>Suaeda monoica</i>	31 nm	Anti-cancer towards human larynx cancer
Kumar <i>et al.</i> , 2015	<i>Andean mora</i>	12-50 nm	Antioxidant, Drug delivery on Hep-G2 cell line cancer cells
Pandian <i>et al.</i> , 2015	<i>Allium sativum</i>	100-800 nm	Anti-cancer
He <i>et al.</i> , 2013	<i>Chrysanthemum morifolium</i>	20-50 nm	Antibacterial
Longhi <i>et al.</i> , 2016	<i>Fusarium oxysporum</i>	-	Antifungal, Biofilm inhibition in <i>Candida albicans</i>
Gupta <i>et al.</i> , 2020	<i>Moringa oleifera</i>	11-25 nm	Anti-cancer activity on human breast cancer, human liver cancer
Sivamaruthi <i>et al.</i> , 2019	<i>Terminalia chebula</i>	20 nm	Antimicrobial, Anti-cancer towards human lung cancer
Lateef <i>et al.</i> , 2016	<i>Cola nitida</i>	17-91 nm	Anticoagulant, Thrombolytic, Larvicidal, Antifungal, Catalytic potential

VII. CONCLUSION

With the demand for nanotechnology and nanomedicine increasing exponentially in the global market, green silver nanoparticles prove to be the perfect theranostic agents. Their lack of toxicity and high biocompatibility make them suitable therapeutic agents of malicious ailments like cancer. Their properties of fluorescence and imaging pave the way for a new era of eco-friendly diagnostic techniques. Even though there are many barriers to the commercial production and use of b-AgNPs, they have a bright future in nanobiotechnology and cancer theranostics. However, the bioavailability, toxicity, compatibility, drug delivery, and body clearance of these b-AgNPs need to be studied thoroughly to evolve and expand their scope in biomedical applications.

CONFLICT OF INTEREST

Authors declare that they do not have any conflict of interest.

REFERENCES

- Abel, B., Coskun, S., Mohammed, M., Williams, R., Unalan, H. E., & Aslan, K. (2015). Metal-enhanced fluorescence from silver nanowires with high aspect ratio on glass slides for biosensing applications. *The Journal of Physical Chemistry C*, 119(1), 675-684.
- Ahmad, M. Z., Akhter, S., Jain, G. K., Rahman, M., Pathan, S. A., Ahmad, F. J., & Khar, R. K. (2010). Metallic nanoparticles: technology overview & drug delivery applications in oncology. *Expert opinion on drug delivery*, 7(8), 927-942.
- Ahmed, M. J., Murtaza, G., Rashid, F., & Iqbal, J. (2019). Eco-friendly green synthesis of silver nanoparticles and their potential applications as antioxidant and anticancer agents. *Drug development and industrial pharmacy*, 45(10), 1682-1694.
- Ahmed, N., Fessi, H., & Elaissari, A. (2012). Theranostic applications of nanoparticles in cancer. *Drug discovery today*, 17(17-18), 928-934.
- AlSalhi, M. S., Devanesan, S., Alfuraydi, A. A., Vishnubalaji, R., Munusamy, M. A., Murugan, K., ... & Benelli, G. (2016). Green synthesis of silver nanoparticles using Pimpinella anisum seeds: antimicrobial activity and cytotoxicity on human neonatal skin stromal cells and colon cancer cells. *International journal of nanomedicine*, 11, 4439.
- Annu, M., Ahmed, S., Kaur, G., Sharma, P., Singh, S., & Ikram, S. (2018). Evaluation of the antioxidant, antibacterial and anticancer (lung cancer cell line A549) activity of Punica granatum mediated silver nanoparticles. *Toxicology research*, 7(5), 923-930.
- Arunachalam, K. D., Arun, L. B., Annamalai, S. K., & Arunachalam, A. M. (2015). Potential anticancer properties of bioactive compounds of Gymnema sylvestre and its biofunctionalized silver nanoparticles. *International Journal of Nanomedicine*, 10, 31.
- Atale, N., Saxena, S., Nirmala, J. G., Narendhirakannan, R. T., Mohanty, S., & Rani, V. (2017). Anti-cancerous effect of albumin coated silver nanoparticles for its protective potential in high glucose-induced cardiac stress: a green approach. *Applied biochemistry and biotechnology*, 181(3), 1140-1154.
- Aziz, N., Faraz, M., Sherwani, M. A., Fatma, T., & Prasad, R. (2019). Illuminating the anticancerous efficacy of a new fungal chassis for silver nanoparticle synthesis. *Frontiers in chemistry*, 7, 65.
- Azizi, M., Ghouchian, H., Yazdian, F., Bagherifam, S., Bekhradnia, S., & Nyström, B. (2017). Anti-cancerous effect of albumin coated silver nanoparticles on MDA-MB 231 human breast cancer cell line. *Scientific reports*, 7(1), 1-18.
- Balakumaran, M. D., Ramachandran, R., & Kalaichelvan, P. T. (2015). Exploitation of endophytic fungus, *Guignardia mangiferae* for extracellular synthesis of silver nanoparticles and their in vitro biological activities. *Microbiological research*, 178, 9-17.
- Barabadi, H., Hosseini, O., Kamali, K. D., Shoushtari, F. J., Rashedi, M., Haghi-Aminjan, H., & Saravanan, M. (2020). Emerging theranostic silver nanomaterials to combat lung cancer: a systematic review. *Journal of Cluster Science*, 31(1), 1-10.
- Bhattacharyya, S. S., Mandal, S. K., Biswas, R., Paul, S., Pathak, S., Boujedaini, N., ... & Khuda-Bukhsh, A. R. (2008). In vitro studies demonstrate anticancer activity of an alkaloid of the plant *Gelsemium sempervirens*. *Experimental Biology and Medicine*, 233(12), 1591-1601.
- Bilal, M., Rasheed, T., Iqbal, H. M., Li, C., Hu, H., & Zhang, X. (2017). Development of silver nanoparticles loaded chitosan-alginate constructs with biomedical potentialities. *International journal of biological macromolecules*, 105, 393-400.
- Brown, A. N., Smith, K., Samuels, T. A., Lu, J., Obare, S. O., & Scott, M. E. (2012). Nanoparticles functionalized with ampicillin destroy multiple-antibiotic-resistant isolates of *Pseudomonas aeruginosa* and *Enterobacter aerogenes* and methicillin-resistant *Staphylococcus aureus*. *Applied and environmental microbiology*, 78(8), 2768-2774.
- Cassano, D., Mapanao, A. K., Summa, M., Vlamidis, Y., Giannone, G., Santi, M., ... & Voliani, V. (2019). Biosafety and biokinetics of noble metals: The impact of their chemical nature. *ACS Applied Bio Materials*, 2(10), 4464-4470.
- Cherukula, K., Manickavasagam Lekshmi, K., Uthaman, S., Cho, K., Cho, C. S., & Park, I. K. (2016). Multifunctional inorganic nanoparticles: Recent progress in thermal therapy and imaging. *Nanomaterials*, 6(4), 76.
- Devi, J. S., & Bhimba, B. V. (2012). Anticancer Activity of Silver Nanoparticles Synthesized by the Seaweed *Ulva lactuca* In vitro. 1: 242. doi: 10.4172/scientificreports.242 Page 2 of 5 Volume 1 • Issue 4 • 2012 silver nitrate solution was added to the filtrate slowly under magnetic stirring conditions for even coating of silver and subjected to heating at 12 C for 10 min. The extract is used as reducing and stabilizing agent for 1mM of Silver nitrate. This one pot green synthesis was the modified method followed by Vigneshwaran et al.[18].
- Dinparvar, S., Bagirova, M., Allahverdiyev, A. M., Abamor, E. S., Safarov, T., Aydogdu, M., & Aktas, D. (2020). A nanotechnology-based new approach in the treatment of breast cancer: Biosynthesized silver nanoparticles using *Cuminum cyminum* L. seed extract. *Journal of Photochemistry and Photobiology B: Biology*, 208, 111902.
- Duran, N., & Seabra, A. B. (2018). Biogenic synthesized Ag/Au nanoparticles: production, characterization, and applications. *Current Nanoscience*, 14(2), 82-94.
- El-Sheekh, M. M., Shabaan, M. T., Hassan, L., & Morsi, H. H. (2020). Antiviral activity of algae biosynthesized silver and gold nanoparticles against Herpes Simplex (HSV-1) virus in vitro using cell-line culture technique. *International Journal of Environmental Health Research*, 1-12.
- Fridman, J. S., & Lowe, S. W. (2003). Control of apoptosis by p53. *Oncogene*, 22(56), 9030-9040.
- Gajbhiye, S., & Sakharwade, S. (2016). Silver nanoparticles in cosmetics. *Journal of Cosmetics, Dermatological Sciences and Applications*, 6(1), 48-53.
- Gardea-Torresdey, J. L., Gomez, E., Peralta-Videa, J. R., Parsons, J. G., Troiani, H., & Jose-Yacaman, M. (2003). Alfalfa sprouts: a natural source for the synthesis of silver nanoparticles. *Langmuir*, 19(4), 1357-1361.
- Gupta, S., Hemlata, H., & Tejavath, K. (2020). Synthesis, characterization and comparative anticancer potential of phytosynthesized mono and bimetallic nanoparticles using *Moringa oleifera* aqueous leaf extract. *Beilstein Arch*, 1, 95.
- Gurunathan, S., Han, J. W., Eppakayala, V., Jeyaraj, M., & Kim, J. H. (2013). Cytotoxicity of biologically synthesized silver nanoparticles in MDA-MB-231 human breast cancer cells. *BioMed research international*, 2013.
- Gurunathan, S., Raman, J., Abd Malek, S. N., John, P. A., & Vikineswary, S. (2013). Green synthesis of silver nanoparticles using *Ganoderma neo-japonicum* Imazeki: a potential cytotoxic agent against breast cancer cells. *International journal of nanomedicine*, 8, 4399.
- He, Y., Du, Z., Lv, H., Jia, Q., Tang, Z., Zheng, X., ... & Zhao, F. (2013). Green synthesis of silver nanoparticles by *Chrysanthemum morifolium* Ramat. extract and their application in clinical ultrasound gel. *International Journal of Nanomedicine*, 8, 1809.
- He, Y., Du, Z., Ma, S., Liu, Y., Li, D., Huang, H., ... & Zheng, X. (2016). Effects of green-synthesized silver nanoparticles on lung cancer cells in vitro and grown as xenograft tumors in vivo. *International journal of nanomedicine*, 11, 1879.
- Heydari, R., & Rashidipour, M. (2015). Green synthesis of silver nanoparticles using extract of oak fruit hull (Jaft): synthesis and in vitro cytotoxic effect on MCF-7 cells. *International journal of breast cancer*, 2015.
- Iravani, S., Korbekandi, H., Mirmohammadi, S. V., & Zolfaghari, B. (2014). Synthesis of silver nanoparticles: chemical, physical and biological methods. *Research in pharmaceutical sciences*, 9(6), 385.

- Jahangirian, H., Lemraski, E. G., Webster, T. J., Rafiee-Moghaddam, R., & Abdollahi, Y. (2017). A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. *International journal of nanomedicine*, 12, 2957.
- Jeelani, S., Reddy, R. J., Maheswaran, T., Asokan, G. S., Dany, A., & Anand, B. (2014). Theranostics: A treasured tailor for tomorrow. *Journal of pharmacy & bioallied sciences*, 6(Suppl 1), S6.
- Jemal, A., Thomas, A., Murray, T., & Thun, M. (2002). Cancer statistics, 2002. *Ca-A Cancer Journal for Clinicians*, 52(1), 23-47.
- Jeyaraj, M., Rajesh, M., Arun, R., MubarakAli, D., Sathishkumar, G., Sivanandhan, G., ... & Ganapathi, A. (2013). An investigation on the cytotoxicity and caspase-mediated apoptotic effect of biologically synthesized silver nanoparticles using *Podophyllum hexandrum* on human cervical carcinoma cells. *Colloids and Surfaces B: Biointerfaces*, 102, 708-717.
- Jeyaraj, M., Sathishkumar, G., Sivanandhan, G., MubarakAli, D., Rajesh, M., Arun, R., ... & Ganapathi, A. (2013). Biogenic silver nanoparticles for cancer treatment: an experimental report. *Colloids and surfaces B: Biointerfaces*, 106, 86-92.
- Jiang, X., Fan, X., Xu, W., Zhang, R., & Wu, G. (2019). Biosynthesis of bimetallic Au-Ag nanoparticles using *Escherichia coli* and its biomedical applications. *ACS Biomaterials Science & Engineering*, 6(1), 680-689.
- Jokerst, J. V., & Gambhir, S. S. (2011). Molecular imaging with theranostic nanoparticles. *Accounts of chemical research*, 44(10), 1050-1060.
- Kadam, J., Dhawal, P., Barve, S., & Kakodkar, S. (2020). Green synthesis of silver nanoparticles using cauliflower waste and their multifaceted applications in photocatalytic degradation of methylene blue dye and Hg 2+ biosensing. *SN Applied Sciences*, 2(4), 1-16.
- Kang, H., Mintri, S., Menon, A. V., Lee, H. Y., Choi, H. S., & Kim, J. (2015). Pharmacokinetics, pharmacodynamics and toxicology of theranostic nanoparticles. *Nanoscale*, 7(45), 18848-18862.
- Karmous, I., Pandey, A., Haj, K. B., & Chaoui, A. (2020). Efficiency of the green synthesized nanoparticles as new tools in cancer therapy: insights on plant-based bioengineered nanoparticles, biophysical properties, and anticancer roles. *Biological Trace Element Research*, 196(1), 330-342.
- Kathiravan, V., Ravi, S., & Ashokkumar, S. (2014). Synthesis of silver nanoparticles from *Melia dubia* leaf extract and their in vitro anticancer activity. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 130, 116-121.
- Kelly, F. M., & Johnston, J. H. (2011). Colored and functional silver nanoparticle- wool fiber composites. *ACS applied materials & interfaces*, 3(4), 1083-1092.
- Khanra, K., Panja, S., Choudhuri, I., Chakraborty, A., & Bhattacharyya, N. (2015). Evaluation of antibacterial activity and cytotoxicity of green synthesized silver nanoparticles using *Scoparia dulcis*. *Nano Biomed. Eng.*, 7(3), 128-133.
- Khanra, K., Panja, S., Choudhuri, I., Chakraborty, A., & Bhattacharyya, N. (2016). Antimicrobial and cytotoxicity effect of silver nanoparticle synthesized by *Croton bonplandianum* Baill. leaves. *Nanomedicine Journal*, 3(1), 15-22.
- Kikuchi, M., Kuroki, S., Kayama, M., Sakaguchi, S., Lee, K. K., & Yonehara, S. (2012). Protease activity of procaspase-8 is essential for cell survival by inhibiting both apoptotic and nonapoptotic cell death dependent on receptor-interacting protein kinase 1 (RIP1) and RIP3. *Journal of Biological Chemistry*, 287(49), 41165-41173.
- Kumar, B., Smita, K., Seqqat, R., Benalcazar, K., Grijalva, M., & Cumbal, L. (2016). In vitro evaluation of silver nanoparticles cytotoxicity on Hepatic cancer (Hep-G2) cell line and their antioxidant activity: Green approach for fabrication and application. *Journal of Photochemistry and Photobiology B: Biology*, 159, 8-13.
- Kuppusamy, P., Ichwan, S. J., Al-Zikri, P. N. H., Suriyah, W. H., Soundharajan, I., Govindan, N., ... & Yusoff, M. M. (2016). In vitro anticancer activity of Au, Ag nanoparticles synthesized using *Commelina nudiflora* L. aqueous extract against HCT-116 colon cancer cells. *Biological trace element research*, 173(2), 297-305.
- Lam, P. L., Wong, W. Y., Bian, Z., Chui, C. H., & Gambari, R. (2017). Recent advances in green nanoparticulate systems for drug delivery: efficient delivery and safety concern. *Nanomedicine*, 12(4), 357-385.
- Lateef, A., Ojo, S. A., Folarin, B. I., Gueguim-Kana, E. B., & Beukes, L. S. (2016). Kolanut (*Cola nitida*) mediated synthesis of silver-gold alloy nanoparticles: antifungal, catalytic, larvicidal and thrombolytic applications. *Journal of Cluster Science*, 27(5), 1561-1577.
- Liang, J., Zeng, F., Zhang, M., Pan, Z., Chen, Y., Zeng, Y., ... & Huang, Y. (2015). Green synthesis of hyaluronic acid-based silver nanoparticles and their enhanced delivery to CD44+ cancer cells. *RSC Advances*, 5(54), 43733-43740.
- Longhi, C., Santos, J. P., Morey, A. T., Marcato, P. D., Durán, N., Pinge-Filho, P., ... & Yamauchi, L. M. (2015). Combination of fluconazole with silver nanoparticles produced by *Fusarium oxysporum* improves antifungal effect against planktonic cells and biofilm of drug-resistant *Candida albicans*. *Sabouraudia*, 54(4), 428-432.
- Madamsetty, V. S., Mukherjee, A., & Mukherjee, S. (2019). Recent trends of the bio-inspired nanoparticles in cancer theranostics. *Frontiers in pharmacology*, 10, 1264.
- Manikandan, R., Manikandan, B., Raman, T., Arunagirinathan, K., Prabhu, N. M., Basu, M. J., ... & Munusamy, A. (2015). Biosynthesis of silver nanoparticles using ethanolic petals extract of *Rosa indica* and characterization of its antibacterial, anticancer and anti-inflammatory activities. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 138, 120-129.
- Maria, B. S., Devadiga, A., Kodialbail, V. S., & Saidutta, M. B. (2015). Synthesis of silver nanoparticles using medicinal *Zizyphus xylopyrus* bark extract. *Applied nanoscience*, 5(6), 755-762.
- Mei, N., Zhang, Y., Chen, Y., Guo, X., Ding, W., Ali, S. F., ... & Chen, T. (2012). Silver nanoparticle-induced mutations and oxidative stress in mouse lymphoma cells. *Environmental and molecular mutagenesis*, 53(6), 409-419.
- Mishra, A., Mehdi, S. J., Irshad, M., Ali, A., Sardar, M., Moshahid, M., & Rizvi, A. (2012). Effect of biologically synthesized silver nanoparticles on human cancer cells. *Science of Advanced Materials*, 4(12), 1200-1206.
- Mukherjee, S., & Patra, C. R. (2017). Biologically synthesized metal nanoparticles: recent advancement and future perspectives in cancer theranostics.
- Mukherjee, S., Chowdhury, D., Kotcherlakota, R., & Patra, S. (2014). Potential theranostics application of bio-synthesized silver nanoparticles (4-in-1 system). *Theranostics*, 4(3), 316.
- Nethi, S. K., Mukherjee, A., & Mukherjee, S. (2020). Biosynthesized Gold and Silver Nanoparticles in Cancer Theranostics. *Handbook of Nanomaterials and Nanocomposites for Energy and Environmental Applications*, 1-15.
- Palai, P. K., Mondal, A., Chakraborti, C. K., Banerjee, I., & Pal, K. (2019). Green synthesized amino-PEGylated silver decorated graphene nanoplateform as a tumor-targeted controlled drug delivery system. *SN Applied Sciences*, 1(3), 1-18.
- Palaniappan, P., Sathishkumar, G., & Sankar, R. (2015). Fabrication of nano-silver particles using *Cymodocea serrulata* and its cytotoxicity effect against human lung cancer A549 cells line. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 138, 885-890.
- Pandian, A. M. K., Karthikeyan, C., Rajasimman, M., & Dinesh, M. G. (2015). Synthesis of silver nanoparticle and its application. *Ecotoxicology and environmental safety*, 121, 211-217.
- Parveen, K., Banse, V., & Ledwani, L. (2016, April). Green synthesis of nanoparticles: their advantages and disadvantages. In *AIP conference proceedings* (Vol. 1724, No. 1, p. 020048). AIP Publishing LLC.
- Patra, S., Mukherjee, S., Barui, A. K., Ganguly, A., Sreedhar, B., & Patra, C. R. (2015). Green synthesis, characterization of gold and silver nanoparticles and their potential application for cancer therapeutics. *Materials Science and Engineering: C*, 53, 298-309.
- Prabhu, D., Arulvasu, C., Babu, G., Manikandan, R., & Srinivasan, P. (2013). Biologically synthesized green silver nanoparticles from leaf extract of *Vitex negundo* L. induce growth-inhibitory effect on human colon cancer cell line HCT15. *Process Biochemistry*, 48(2), 317-324.
- Qasim Nasar, M., Zohra, T., Khalil, A. T., Saqib, S., Ayaz, M., Ahmad, A., & Shinwari, Z. K. (2019). Seripeidum quettense mediated green synthesis of biogenic silver nanoparticles and their theranostic applications. *Green Chemistry Letters and Reviews*, 12(3), 310-322.
- Ramar, M., Manikandan, B., Marimuthu, P. N., Raman, T., Mahalingam, A., Subramanian, P., ... & Munusamy, A. (2015). Synthesis of silver nanoparticles using *Solanum trilobatum* fruits extract and its antibacterial, cytotoxic activity against human breast cancer cell line MCF 7. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 140, 223-228.
- Rauwel, P., Küüna, S., Ferdov, S., & Rauwel, E. (2015). A review on the green synthesis of silver nanoparticles and their morphologies studied via TEM. *Advances in Materials Science and Engineering*, 2015.
- Reddy, N. J., Vali, D. N., Rani, M., & Rani, S. S. (2014). Evaluation of antioxidant, antibacterial and cytotoxic effects of green synthesized silver nanoparticles by *Piper longum* fruit. *Materials Science and Engineering: C*, 34, 115-122.
- Sahoo, A. K., Goswami, U., Dutta, D., Banerjee, S., Chattopadhyay, A., & Ghosh, S. S. (2016). Silver nanocluster embedded composite nanoparticles for targeted prodrug delivery in cancer theranostics. *ACS Biomaterials Science & Engineering*, 2(8), 1395-1402.
- Salvadori, M. R., Ando, R. A., & Corrêa, B. (2022). Bio-separator and biosynthesizer of metallic nanoparticles-A new vision in bioremediation. *Materials Letters*, 306, 130878.
- Satyavani, K., Gurudeban, S., Ramanathan, T., & Balasubramanian, T. (2011). Biomedical potential of silver nanoparticles synthesized from

- calli cells of *Citrullus colocynthis* (L.) Schrad. *Journal of nanobiotechnology*, 9(1), 1-8.
- Satyavani, K., Gurudeeban, S., Ramanathan, T., & Balasubramanian, T. (2012). Toxicity study of silver nanoparticles synthesized from *Suaeda monoica* on Hep-2 cell line. *Avicenna journal of medical biotechnology*, 4(1), 35.
- Sharma, D., Ledwani, L., & Bhatnagar, N. (2015). Antimicrobial and cytotoxic potential of silver nanoparticles synthesized using *Rheum emodi* roots extract. *New Frontiers in Chemistry*, 24(2), 121.
- Shawkey, A. M., Rabeh, M. A., Abdulall, A. K., & Abdellatif, A. O. (2013). Green nanotechnology: anticancer activity of silver nanoparticles using *Citrullus colocynthis* aqueous extracts. *Adv. Life Sci. Technol*, 13, 60-70.
- Sivamaruthi, B. S., Ramkumar, V. S., Archunan, G., Chaiyasut, C., & Suganthi, N. (2019). Biogenic synthesis of silver palladium bimetallic nanoparticles from fruit extract of *Terminalia chebula*—In vitro evaluation of anticancer and antimicrobial activity. *Journal of Drug Delivery Science and Technology*, 51, 139-151.
- Srinoi, P., Chen, Y. T., Vittur, V., Marquez, M. D., & Lee, T. R. (2018). Bimetallic nanoparticles: enhanced magnetic and optical properties for emerging biological applications. *Applied Sciences*, 8(7), 1106.
- Sukirtha, R., Priyanka, K. M., Antony, J. J., Kamalakkannan, S., Thangam, R., Gunasekaran, P., ... & Achiraman, S. (2012). Cytotoxic effect of Green synthesized silver nanoparticles using *Melia azedarach* against in vitro HeLa cell lines and lymphoma mice model. *Process Biochemistry*, 47(2), 273-279.
- Tiquia-Arashiro, S., & Rodrigues, D. (2016). Application of nanoparticles. In *Extremophiles: Applications in Nanotechnology* (pp. 163-193). Springer, Cham.
- Ullah, I., Khalil, A. T., Ali, M., Iqbal, J., Ali, W., Alarifi, S., & Shinwari, Z. K. (2020). Green-synthesized silver nanoparticles induced apoptotic cell death in MCF-7 breast cancer cells by generating reactive oxygen species and activating caspase 3 and 9 enzyme activities. *Oxidative medicine and cellular longevity*, 2020.
- Vanaja, M., Paulkumar, K., Baburaja, M., Rajeshkumar, S., Gnanajobitha, G., Malarkodi, C., ... & Annadurai, G. (2014). Degradation of methylene blue using biologically synthesized silver nanoparticles. *Bioinorganic chemistry and applications*, 2014.
- Varghese Alex, K., Tamil Pava, P., Rugmini, R., Shiva Prasad, M., Kamakshi, K., & Sekhar, K. C. (2020). Green synthesized Ag nanoparticles for bio-sensing and Photocatalytic applications. *ACS omega*, 5(22), 13123-13129.
- Vedelago, J., Gomez, C. G., Valente, M., & Mattea, F. (2018). Green synthesis of silver nanoparticles aimed at improving theranostics. *Radiation Physics and Chemistry*, 146, 55-67.
- Venkatesan, B., Subramanian, V., Tumala, A., & Vellaichamy, E. (2014). Rapid synthesis of biocompatible silver nanoparticles using aqueous extract of *Rosa damascena* petals and evaluation of their anticancer activity. *Asian Pacific journal of tropical medicine*, 7, S294-S300.
- Venugopal, K., Ahmad, H., Manikandan, E., Arul, K. T., Kavitha, K., Moodley, M. K., ... & Bhaskar, M. (2017). The impact of anticancer activity upon *Beta vulgaris* extract mediated biosynthesized silver nanoparticles (ag-NPs) against human breast (MCF-7), lung (A549) and pharynx (Hep-2) cancer cell lines. *Journal of Photochemistry and Photobiology B: Biology*, 173, 99-107.
- Venugopal, K., Rather, H. A., Rajagopal, K., Shanthi, M. P., Sheriff, K., Illiyas, M., ... & Maaza, M. (2017). Synthesis of silver nanoparticles (Ag NPs) for anticancer activities (MCF 7 breast and A549 lung cell lines) of the crude extract of *Syzygium aromaticum*. *Journal of Photochemistry and Photobiology B: Biology*, 167, 282-289.
- Vijistella Bai, G. (2014). Green Synthesis Of Silver Nanostructures Against Human Cancer Cell Lines And Certain Pathogens. *International Journal of Pharmaceutical, Chemical & Biological Sciences*, 4(1).
- Xie, Z., Su, Y., Kim, G. B., Selvi, E., Ma, C., Aragon-Sanabria, V., ... & Yang, J. (2017). Immune Cell-Mediated Biodegradable Theranostic Nanoparticles for Melanoma Targeting and Drug Delivery. *Small*, 13(10), 1603121.
- Yetisgin, A. A., Cetinel, S., Zuvun, M., Kosar, A., & Kutlu, O. (2020). Therapeutic nanoparticles and their targeted delivery applications. *Molecules*, 25(9), 2193.
- Yhee, J. Y., Son, S., Kim, N., Choi, K., & Kwon, I. C. (2014). Theranostic applications of organic nanoparticles for cancer treatment. *Mrs Bulletin*, 39(3), 239-249.
- Zavaleta, C., Ho, D., & Chung, E. J. (2018). Theranostic nanoparticles for tracking and monitoring disease state. *SLAS TECHNOLOGY: Translating Life Sciences Innovation*, 23(3), 281-293.
- Zeedan, G. S. G., EL-Razik, K. A. A., Allam, A. M., Abdalhamed, A. M., & Zeina, H. A. A. (2020). Evaluations of potential antiviral effects of green zinc oxide and silver nanoparticles against bovine herpesvirus-1. *Adv. Anim. Vet. Sci*, 8(4), 433-443.