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Research Paper

Anticancer Potential of Silver Nanoparticles by Using Lantana Camara Leaf

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ABSTRACT

At present, green synthesized based delivery systems play a major role in the bio medical field. Lantana camara, also known as Unnichedi in Tamil, is an evergreen shrub that is involved in a variety of cancer diseases due to its pharmacological activity. In additions, the leaf extracts of Lantana camara was found to have excellent anti-cancer activity. The green synthesized AgNPs of Lantana camara leaves extract were more efficient against oral cancer. In the report, green synthesized nano-formulations in presence of AgNPs were formulated. The as prepared formulation was confirmed by UV spectroscopy, particle size and zeta potential, scanning Electron Microscopy (SEM). In UV spectroscopy the absorbance of the peak appears between the range of 200 to 300 nm corresponding to the formulation of AgNPs. The zeta potential shows high colloidal stability; the average potential value is -12.6Mv. The particle size results shown that the average size of AgNPs is 268.1 nm. The morphology and particle size determined using SEM analysis indicate spherical shaped particles. Further, the oral anti-cancer activity was evaluated on squamous cell cancer (SCC-25) CELL LINE. The cell line result shown is that the IC 50 Value for AgNPs was 39µg/ml and the plant extract shown 145µg/ml, this indicates that the silver nanoparticles have more potential when compared to the leaf extract

INTRODUCTION

Plants are a vital source of medicinal compounds. Also, many health issues were treated with medicinal herbs in antiquity. The examination of plants yields a wide range of bioactive compounds. Numerous plants have been studied and reported on for a variety of therapeutic properties.[1] *Lantana camara* is also known as *Lantana*.[2] it is a flowering ornamental plant. It belongs to the family: Verbenaceae, a kingdom: planate, division:

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Magnoliopsida, Order: Lamiales, genus: *Lantana*, species: *Lantana camara*Linn shown in Figure 1. It is commonly called as "unnichedi" in Tamil.[3]*Lantana* sp. (Verbenaceae) is a highly invasion tropical weed that attacks more than 60 % of forests worldwide.[4] The genus harbors 150 species and is native to the tropical and subtropical areas of South America, Asia, and Africa. *L.camara*is the most dominant species.[5] Although *Lantana* sp. Is used in many countries as decorative ornamental, the presence of pentacyclictriterpenoids, including lantadenes A and B in their leaves and seeds, has been correlated with the plants adverse effects, especially when ingested by animals, causing cholestasis, hepatotoxicity, and phototoxicity.

Taxonomic Classification[6]:

Kingdom : plantae

Subkingdom : Tracheobionta

Super division : Spermatophyta

Division : Magnoliopdida.

Subclass : Asteridae

Order : Lamiales.

Figure 1: Lantana camara plant

Family : Verbenaceae

Genus : *Lantana*

Species : *Camara*.

Vernacular names: English name - Wild sage; Hindi – caturang

Malayalam - Arippochedi; sanskrit – Caturangi, Vanacchedi; Kannada – Chitrangi.[7]

Nanoparticles:

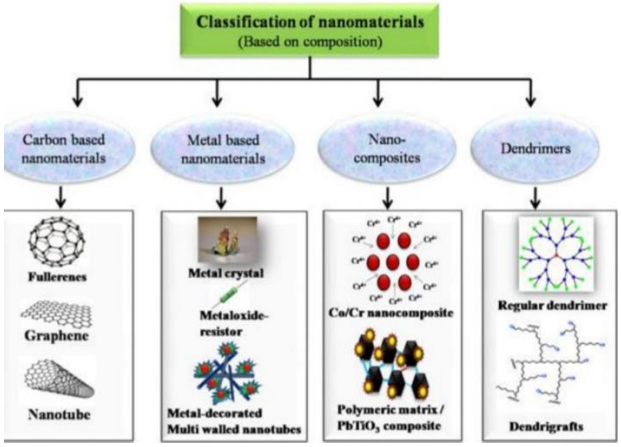

Figure 2: Synthesis of silver nanoparticles using fresh leaves of Lantana camara

Nanopaticles represent a particle with a nanometer size of 1-100 nm. The nanoscale material has new, unique, and superior physical and chemical properties compared to its bulk structure, due to an increase in the ratio of the surface area per volume of the material/particle.[8]The most widely studied nanoparticle materials are metal nanoparticles because they are easier to synthesize. Moreover, these materials have a wide range of applications: detectors, catalysts, surface coating agents, and antibacterial/antimicrobials, among many others. Some of the most studied matallic nanoparticles include silver (Ag).[9-10],gold (Au)[11-12],platinum(Pt)[13-14]and palladium (Pd).[15]The nanoscale material due to an increase in the ratio of the surface area per volume of the material/particle. The material has unique, new and superior chemical and physical properties when compared to its bulk structure.[16] Even though the methods involved in synthesis of

nanoparticles results in different anticipated characteristics of a particles, the physical and chemical methods include lithography, ultrasonic fields, UV irradiation and photochemical reduction processes for the synthesis of nanoparticles have their own pitfalls while they are costly, labour-intensive, and toxic to both organisms and the environment.[17-18]

Figure 3 : Silver nanoparticles

- silver nanoparticles can be synthesized by several methods like chemical. reduction. since the chemical reduction methods are economical and easier to prepare these are most commonly used.[19]
- But the use of chemicals in the synthesis of Ag nanoparticles result in the adsorption of toxic chemicals on the surface of the material so that it will have adverse and harmful effects application.[20]

Cancer:

A cancer that start in the tissues of the mouthor throat is called oral cancer.[21]oral cancer is affectedby the various bio-environmental factors such as fatal illness, and in the mouth, it might result in plaques, foulbreath, or ulcers. Makeover, coughing and swallow lymph nodes in the neck are typical signs.[22] The Lantana camara Linn plant is being studied for its potential as an oral anticancer because of its inherent ability to treat mouth ulcers. Squamous cell cancer makes up more than 90% of oral and oropharyngeal cancer cases. [23]Cancer is a serious hazard to human health, and it causes death to millions of people's worldwide annually. In Iraq, the cancer registry reported more than twenty thousand newly diagnosed cancer cases in 2012. [24] Hence, green synthesis of AgNPs using leaf extracts of Lantana camara might be an effective drug for oral cacer.The pharmacological activity of L. *Camara* is shown in Figure 4. [25]

Figure 4 :Pharmacological activities of *L. camara*.

Treatment Of Cancer :

Cancer is a life-threatening disease that is characterized by the continuous growth of cells. There are a number of drugs are available chemically for the treatment of cancer such as imatinib, gefitinib, rituximab, bevacizumab, lapatinib etc. Chemotherapeutic approach followed to kill cancerous cells by inhibiting the process of cell division. But this approach is successful for highly developed stages of cancer

because drugs can reach the site of cancer cells with reduced specifically. Hence the concept of nanoscale devices is designed to develop biodegradable self-assembled nanoparticles, which are used for targeting the delivery of anticancer drugs. [24]Nanotechnology is gaining popularity in research that leads to the development of sophisticated, multifunctional, novel approaches which can recognize cancer cells and deliver drugs to target organ or tissue and help to prevent precancerous cells from becoming malignant. [26]

Nanotechnology In Reduction of Obesity:

Nanotechnology can be used as a powerful public health tool for the provision of low calorie food which plays an important role in controlling obesity. Nanotechnology based food and products and food packaging materials are provided to consumers in some countries. [27]

Nanotechnology In Diagnosis:

Carbon Nanotubes: carbon nanotubes are designed based on bisectors and employed for the detection of analytes in the Healthcare system. It's also used for monitoring an detection of amino sugars, protein, albumin sugars, amino acids, immunoglobulin, neurotransmitters, insulin and human chronic gonadotropin etc. These are categorized into different types such as single walled, Double-walled and multi walled carbon nanotubes. SWNTs are characterized by strong covalency bonding, one – dimensional structure and nanometer size of 0.4-2 nm. The electrical and mechanical Properties of SWNTs may change due to breaking of C= C bond during chemical processes. DWNTs are made up of a pristine carbon nanotube core and chemically functionalities naotube shells. DWNTs in biological system are used as imaging and therapeutic agents. MWNTs consist of concentric tubes with multiple rolled layers of graphene. [28-29]

Graphenes : It consists of thin layer of tightly packed carbon atoms and bonded all together in A hexagonal honeycomb. It is used in diagnostics nd biosensors due to its considerable Properties like high mechanical strength**,** good thermal conductivity, elevated elasticity, and optical Properties. It is a transparent substance with a very low production cost and environmentally friendly mainly helpful for the identification of biological samples such s glucose, hemoglobin, cholesterol, dopamine, uric acid. [30-31]

Quantum Dots : These sre inorganic nanocrystals which are prepared I. Between 3 and 15 nm and suitable for binding with specific biomolecules. They have unique optical Properties like narrow emission spctra, broad excitation, high photochemical stability, and less photo bleaching. It is used for the development of optical biosensors to identify organic compounds, ions, and biomolecules such as nucleic acids, amino acids, proteins, enzymes, sugars and neurotransmitters. [32-33]

Phytochemical Analysis of Lantana Camara: [34]

1. Carbohydrates
2. Saponin
3. Tannins
4. Glycosidic
5. Flavonoids
6. Phenols
7. Proteins
8. Triterpenoids
9. Quinolones.

Nanotechnology In Drug Delivery System:

The drug delivery system significantly produces an impact on the use of drugs in patients. This system should minimize the side-effects and also reduce both the dose and frequency of dosage. Due to thir small size and large surface area there is a large saffinity for drugs and small molecules like antibodies or ligands for targeting specific diseases and releasing therapeutic agents at the controlled rate. [35-36]

Emerging Scenario of Nanoparticles:

The advancement in naotechnology will lead to innovative synthetic routes along with new processing stratergies with economical manufacturing process. So the required for new drug development in the area of nanotechnology can be reduced which can save humn lives. [37-38] In coming year's nanotechnology will play a significant role in the health care system to provide an innovative prospect for early detection in diseases, diagnostic and remedial measures to improve health condition and also enabling precise and effective therapy tailored to the patients. [39-40]

Current And Future Development:

Currently various investigations are carried out on nanotechnologies to utilize its application in the field of therapeutic, diagnostic and drug delivery systems. In recent times, nano-based drug delivery systems are applied to facilitate the successful delivery of drugs into the target sites. Generally, the main targets in the body system are the receptors or proteins on cell membranes and cell surfaces respctively. Na notechnology will play a key role to revolutionize medicine in future developments. The nano robotic tools can be applicable in the treatment of various cardiovascular diseases and atherosclerosis by the year 2028. [41-42]

Useful Parts of The Plant:

Lantana camara is ornamental plant, but due to the presence of various phytoconstituents, it has been used as a traditional medicine for an extended time. Generally, the parts use are leaves, flowers, Root, and Whole plant. [43]

Figure 5 : Plant *Lantana camara*

Figure 6 : Leaves of *Lantana C.*

Figure 7 : Flower of *Lantana C*

Figure 8 : fruit of *lantana C.*

Phytochemistry Of the Drug:

Table 1 : phytochemistry of the drug[44-45]

Part	Chemical constituents
Seed	Organic matter, 95.2; crude protein,6.6; ether extract, 2.4; N-Free extract, 55.4; Crude fire,30.7; Total ash,4.8; total phenolic substances, 3.45%.
Aerial part	Triterpenoids, camarilic acid, camaracinic acid, lantadene A and ursolic, betulinic and oleanolic acids .

Leaves	Flavanol glycoside, camaraside, phenylpropanoid glyciside, lantanaside, lantoic acid, lantanilic acid, verbascoside. Lantadene A and B, steroid lancamarone, volatile oil lantanol
Flower	Volatile oil, anthocyanin
Dried flower	Volatile oil, 0.07%
Bark of stem and root	Quinine like alkaloid lantanine.

Traditional Uses:

- Locally the traditional healers from Dakshin kannada district of karnataka use pounded leaves and leaf juice to manage cuts, ulcers, and swellings.
- Taila is prepares by adding the decoction of both *Lantana camara* leaves, and *Eupatorium odoratum* is used for external application for the wound.
- The decoction of leaves and fruits is used as a lotion for wounds.
- Decoction of the leaves is used for the vitiated condition of vata and kapha.
- In case of eczema and eruption, a decoction of the leaves is used internally in the dose of 10-20ml twice a day, along with an external application of leaf paste.
- The leaf juice /decotion is used for gargling in mouth ulcers.
- Malaria-leaf juice internally in the dose of 20ml twice daily.
- For sparin and contusion, pounded fresh leaves are applied as a poultice.
- For rheumatism, oil is spread on leaves, warmed, and applied to the affected part.[46-47]

Pharmacological Activites of Lantana Camara L.:

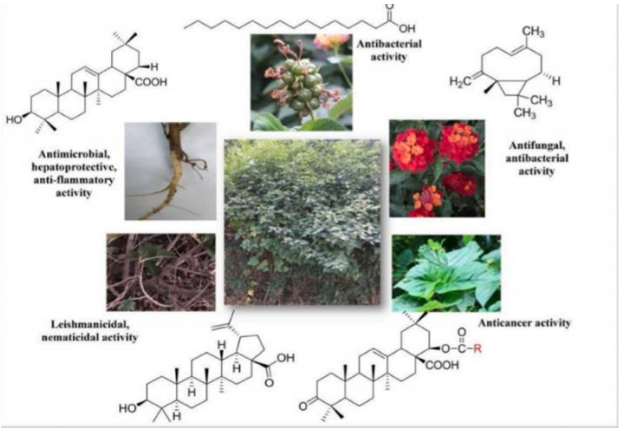

Figure 5 : Lantana camara and its compounds.

Antibacterial activity:

Ethanolic extracts of *Lantana camara* leaves and roots were reported for antibacterial activity. Microdilution method is performed for in-vitro antibacterial activity. The extracts exhibited antimicrobial activity against *stephyloccus aureus*, *proteus vulgaris*, *pseudomonas aeruginosa*, Escherichia coli, *Vibrio cholareae* and two multiresistant stains *E.coli* and *S. aureus.*

Antifungal activity:

The lantana *camara* extracts of hot water and ethanol is screened for its activity against wood destroying white and brown fungi. Through the both extracts resulted in efficient white and brown antifungal activity. But, the ethanol extract at very low concentration about 0.01% was showned to have highly potential antifungal activity.

Hemolytic activity:

The hemolytic activity of *lantana camarais* perfomed by using aqueous extract. The solvent fractions of different concentrations were taken [125,250,500,1000 µg/ml] using spectroscopic method. The aqueous extract and its solvent fractions exihibited very low hemolytic activity towards human erythrocytes. The haemolytic activity of the different extracts was found in order : chloroform fraction > hexane and ethyl acetate frection > aqueous extract > ethanol fraction > methanol fraction.

Antimotility activity:

Methanol extract of Lantana. camara leaves was reported antimotility activity in mice. Intestinal motility assayed by charcoal meal test in mice. A dose of 1 g/kg body weight extract completely inhibited the transit of charcoal in mice. Intraperitoneal administration of 125mg/kg and 250 mg/kg body weight the extracts significantly reduced the fecal output in castor oil induced diarrhoea in mice.

Anti mutagenic activity:

22β-dimethylacryloyloxy and 22β- acidacetoloxy lantanolic acid from L. camara showed antimutagenic activity. The antimutagenicity test performed by micro-nucleus test in Swiss mice. High anti mutagenic activity is exhibited by both of the compounds in Mitomycin - C induced mutagenesis in mice.

Antioxidant activity:

The leaves of Lantana camara was reported by reducing power activity and 1,1- diphenyl-2-picrylhydrazyl by radical scavenging assay. The antioxidant activity is exhibited by the leaves. .younger leaves shown to exhibit stronger antioxidant activity when compared to matured or older leaves.

Antiurolithiatic activity:

The leaves of Lantana camara ethanolic extract was reported for antiurolithiatic activity against ammonium and chloride ethylene glycol induced calcium oxalate urolithiasis in male albino rats. Extract treatment significantly reduced the deposition of calcium; oxalate and also decreased urinary excretion of calcium; oxalate and creatinine.

Mosquito controlling activity:

Mosquito larvicidal activity of ethanol and methanol extracts of leaves and flowers of Lantana camara were reported against 3rd and 4th instar larvae of Ae. aegypti and Cx. quinquefasciatus mosquito. Both extracts exhibited significant larvicidal activity against both species of mosquitoes; however, at low concentrations extracts were highly active against Ae. aegypti than that of Cx. Quinquefasciatus.[48]

Toxicity Of Lantana Camara:

Lantana is one among the most toxic plants known so far possibly within top ten. Reports of *lantana camara* toxicity have been sated from India. America, Australia, New Zealand, South Africa. The consumption of high amount of plants material leads to toxicity. It is reported that goats, sheep and cattle are susceptible to lantadenes A,B,C and iatrogenic acid toxicity were as rats, horses, neonatal calves and lambs are not susceptible to lantadene A. The prominent clinical sigh of poisoning includes jaundice and photosensitization. Loss of appetite in poisoned animals occurs within 24-prominent clinical sign of in appetite is also observed, most severely poisoned animals die within 2-days of poisoning but usually death occurs after 1-3 weeks after poisoning. The kidneys are pale in colour and swollen, the gall bladder is grossly distended and the liver is enlarged. The oral toxic dose of lantadene A for sheep is 60mg/kg is toxic and 1-3 mg/kg by intravenous route.[49-50]

CONCLUSION:

Due to the advancement of science and technology, there is a tendency to ignore traditional knowledge and medicine. Documantation of this valuable traditional

knowledge through ethnobotanical studies is essential for conserving natural resources. *Lantana camara* L. Belonging to the family Verbenaceae, is considered an invasive weed worldwide. It is quite obvious that from this review Lantana camara used for numerous therapeutic purposes different types of nanoparticles extracted from this even individual part have own therapeutic benefits such as cardiovascular diseases, atherosclerosis anti cancer, anti viral etc. Nanotechnology will play a key role to revolutionize medicine in further development.

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