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Review Article

Review on *Callilstemon citrinus*: Recent Approaches in Novel Drug Delivery System

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Abstract

Callistemon citrinus is an ornamental plant. The plant is commonly originated in subtropical and tropical region. C.citrinus, commonly referred to as bottlebrush, is a member of myrtaceae family. Active ingreadients such as 1, 8-cineole, triterpenoids, α-pinenes, eucalyptol, tannis, alkaloids, flavonoids, saponins, phytosterol etc. are mostly found in the various plant sections. It is generally use in traditional, folk and herbal medicine as a water accent, anticough, antibronchtits, insecticide and treatment of diarrhoea, dysentery and rheumatism. This article aims to provide a comprehensive review on the pharmacological aspects and recent novel approaches of callistemon citrinus highlight methodologies, applications, and potential contributions of this natural extract in enhancing drug delivery, offering insights into its pharmacological potential and future prospects in the field. The primary objective to collect updated information about effectiveness of the plant extract in addressing specific health issues and its potential as a therapeutic effect using novel drug delivery systems. Innovative methods explored in delivering the plant extract, such as Nano formulations in various diseases i.e. Antifungal properties, acute toxicity, brine shrimp cytotoxicity and relaxant activity, antimicrobial Activity etc. The methods improve therapeutic efficacy and reduces side effects by optimizing the delivery of bioactive compounds from callistemon citrinus.

Keywords: Callistemon citrinus, Bottle brush, Pharmacological activities, Novel Drug Delivery Systems, Isolated compounds.

1. Introduction:

From the beginning of human civilization, plants and products derived from plants are used as a source of medication to cure a many of the diseases. The use of plants in conventional medicine is explained by a number of traditional medical systems. Plants are a source of chemical substances that have been used as medicines and as a source of novel lead molecules for contemporary synthesis and design[1]. Callistemon citrinus L, popularly referred to as "red bottle brush," is one of those most significant medicinal herbs. The plant's name, Callistemon, comes from the Greek words kalos, which means lovely, stemon, which means stamens, and citrinus, which comes from the Latin word citrinus, which means lemon and refers to the aroma of the leaves. This evergreen tree is a member of the Myrtaceae family. It grows native in Queensland and New South Wales and is grown in gardens all throughout India. It is occasionally used similarly with Melaleuca. Because of its cylindrical, brush-like blossoms that resemble classic bottle brushes[2], the plant is popularly referred to as bottle brush. India's rural population uses various portions of the plant. The plant's volatile oil has been utilised as an antibacterial and antifungal agent, it is known to use in the folk medicine as anticough, antibronchitis and insecticidal properties[3]. Furthermore, ethnic tribal people usually use the aerial portions of Callistemon citrinus, and nothing is known about its scientific significance. Callistemon citrinus was an evergreen plant with aromatic, alternating, lanceolate leaves that had an entire border and anomocytic stomata. The stem had a grey colour. A phytochemical analysis of leaves shows the presence of steroids, flavonoids, alkaloids, and terpenoids[4].

1.1 Classification:

Kingdome: Plantae

Class: Dicotyledons

Subclass: Rosidae

Family: Myrtaceae

Genus: Callistemon

Species: Callistemon Citrinus Curtis

1.2 Vernacular names:

Engllish: Crimson Bottlebrush

Hindi: Cheel, Kastula

Marathi: Jhankara, Kateri

Tamil: Palasu

Sanskrit: Naahlingam

Kannada: Muthuga

Punjabi: Palak Chachra Oriya Polaso

1.3 Cultivation:

This little ornamental tree is grown all year round in India in gardens, avenues, and roadside plantings. This species flowers

twice a year in Agra, Uttar Pradesh, and northern India (February–May and August–November)

Parameters of cultivation: Full sun is required for light. Tolerances for soil: loam, sand, clay, acidic, well-drained High tolerance to dry conditions

Callistemon citrinus, commonly known as the crimson bottlebrush, contains various compounds in its different parts:

Flowers: Anthocyanins (cyanidine 3,5-O-diglucoside, peonidin 3,5,O-glucoside, cyanidine-3-O-glucoside, cyaniding-coumaroylglucoside-pyruic acid

Fruit: α-amyrin, α-terpineol, β-sitosterol, oleanolic acid, 1, 8-cineol

Seeds: Gallic acid, ellagic acid

Leaves: Gallic acid, Rutuine, 1, 8-cineole, limonene, alpha terpinol, alpha pinene, Beta terpinene, P-cymene, steroids, carbohydrates, quercetin, ellagic acid, flavonoids, P-coumeric acid

Steam: Anthraquinone, Flavonoids (5,4-dihydroxy-6-C-methoxy flaonone, 5,4-dihydroxy-8-c-methyl-7-methoxy) Saponins, Tannins (3,3-di-O-methyl ellagic acid, 3,3,4-tri-O-methyl ellagic acid, ellagic acid XIX) Alkoloids, phlobatannins, reducing sugers

2. Pharmacological activities:

2.1 Antimicrobial action:

The leaves of C. citrinus have broad-spectrum antibacterial properties against a variety of bacteria and fungi. The examined bacteria's ability to multiply was decreased in methanolic extract of leaves. Furthermore, 64% of the studied bacteria were stopped from growing by floral extracts. It shows that leaves extract were most effective than gram negative bacteria against gram-positive bacteria[5]. Alkaloids isolated from C. citrinus exhibited antibacterial action in addition to blocking ATP-dependent molecules from passing through cell membranes. Alkaloids are thus considered to be possibly antibacterial plant components[6].

2.2 Cardioprotective effect:

Doxurubicine induced cardiotoxicity in rats, C.citrinus extract had a strong cardioprotective effect. Blood preaaure and heart rate were decreased by doxorubicin. In contrast, the C.citrinus leaves extract shows the normal leavels of systolic, diastolic, mean blood pressure and heart rate[7].

2.3 Antidepressant effect:

The chloroform fraction of C.citrinus exhibited antidepressant effect equivalent to that of imipramine (10mg/kg), the standard medication. As previously indicated, C. citinus is rich in bioactive chemicals, the bulk of which are terpenoids and flavanoids, which have antidepressant properties[8].

2.4 Anti-diabetic effect:

Diabetes induced by streptozotocin in experimental animals, Fraction of petroleum ether, chloroform and ethanol of C.citrinus leaves shows the antidiabetic potential. Futher some negative effects, C.citrinus treatment show the increase in levels of GSH and antioxidant enzymes and lipid peroxidation in diabetic rats. When 400 mg/kg of C.citrinus methanolic fruit exract was administerd to diabetic rats induced with alloxan, a notable antidiabetic effect was seen. In rats with diabetes caused by alloxan, extracts from C.citinus leaves also improved the liver profile, body weight, total lipid content, and renal profile[9].

2.5 Antitubercular activity:

The chloroform extract of C.citrinus were effective against both resistant and pan-sensitive strain of tuberculosis. This gave justification for development of C.citrinus chloroform extract as medications to treat multidrug-resistant tuberculosis[10].

2.6 Anti-inflammatory activity:

Strong anti-inflammatory properties were demonstrated by the methanolic extact of C. citrinus leaves. At 400 mg/kg, the methanolic leaf extract of C. citrinus had anti-inflammatory action that was remarkably similar to that of the conventional medication diclofenac sodium[11].

2.7 Antifungal, antioxidant, and antiaflatoxin properties:

Numerous investigations looked at the antifungal, antioxidant, and antiaflatoxin properties of C. lanceolatus sweet essential oil. Following gas chromatography-mass spectroscopy examination, the essential oils of C.lanternifolius were found to contain eight compounds in total, with 8-cineole accounting for the majority of these. The presence of 1,8-cineol in the essential oil was responsible for its antifungal action, as demonstrated by a contact assay conducted on Czapek's dox agar. Strong elastase inhibition and DPPH radical scavenging capabilities were observed in the ethanol extracts of C. citrinus[12].

2.8 Calcium channel blocking action:

On rabbit jejunum preparations isolated, it was discovered that the fruit methanolic extracts of C. citrinus exhibited antispasmodic effect. This extract has been shown to have a calming effect on the jejunum of rabbits when it contracts naturally. By inhibiting their calcium channels, the fruits of C. citrinus had an antispasmodic effect on the rabbit's jejunum. Additionally, Callistemon citrinus syn. Callistemon lanceolatus shown anti-bacterial, anti-helicobacter pylori, hypoglycemic, spasmolytic, antioxidant, and hepatoprotective properties[13].

2.9 Acute toxicity, cytotoxicity and relaxant activity:

To identify the bioactive chemicals and trace the spasmolytic elements of C. citrinus Curtis's crude methanol extract, fractions were screened. Standardisation tests were also conducted on the crude methanol extract's acute toxicity and cytotoxicity. The ethylacetate fraction had the highest concentration of relaxant components, followed by n-butanol, chloroform, and aqueous fraction which supported its isolation. The result of cytotoxic assay suggest that the plant species may be a source of cytotoxic compound, and the crude methanol extract was safe at concentration of 250 mg/ml or less[14].

2.10 Antifungal properties:

Characteristics that inhibit fungal growth essential oils are extracted through hydrodistillation from the leaf of four cameroonian Myrtaceae species C.rigidus, C.citrinus, Eucalyptus camaldulensis and Eucalyptus saligna were found to have antifungal activity against Aspergillus flavus. The antifungal activity of the steam-distilled leaf essential oils of Callistemon citrinus and Callistemon citrius against Phaeoramularia angolensis was determined. 1,8-cineole predominated in the oils of Callistemon rigidus and Callistemon citrinus, with 79.1% and 73.8% of each species, respectively[15].

2.11 Antibacterial activity:

Using the disc diffusion method, the antibacterial properties of ethanolic and methanolic extracts of callistemon citrinus and Albizia lebbeck leaves were investigated against a variety of pathogenic bacteria, including S.typhi, Kelebsiella Pneumoniae, Streptoccocus epidermidis, Escherichia coli,

Pseudomonas aeruginosa and Listeria monocytogenes. The ethanolic and methanolic extracts had strong antibacterial efficacy against bacteria, according to their findings. Its effectiveness against S. typhi, B. cereus, S. epidermidis, and B. anthracis is particularly noteworthy and is comparable to that of antibiotics. It is also evident that the plant extract has a positive effect on resistant P. aeruginosa bacterium. Additionally, these extracts have a more noticeable effect on gramme positive bacteria than gramme negative bacteria. According to the study's findings, C. citrinus is a potent antibacterial plant that can be utilised in folk medicine and that will be useful resource for the discovery of novel antimicrobial drugs for the treatment and management of diseases[16].

2.12 Antiprolifertive action:

Action that inhibits proliferation one possible approach to cancer prevention is the ongoing hunt for innovative and potent medications derived from medicinal plants. By decreasing the production of reactive oxygen species, lowering cell growth, and preventing cell migration, the ethyl acetate and methanol extracts of Callistemon lanceolatus leaves had a strong antiproliferative impact aganinst HepG2 liver cancer cells. Additionally, pretreatment of HepG2 cells with both extracts resulted in a considerable suppression of the expression of signal transducer and activiator of transcription3, upregulation of p53, and inhibition of cyclin A and cdk2 activities[17].According to[18], the ethyl acetate extract and partially purified components from C.lanceolatus leaf demonstrated encouraging antiproliferative efficacy against HeLa cell lines. In ovarian cancer cells such as ES2 and OV90 cells, a C-methylated flavone called sideroxylin that was isolated from callistemon lanceolatus effectively reduced cell proliferation and increased apoptosis by inducing mitochondrial dysfunction and activating phosphoinositide 3-kinase and mitogen-activated protein kinase signal transduction[19].

2.13 Insecticidal activity:

The more destructive insect pest in stored pulses is the Callosobruchus chinensis L. (pulse beetle) in Asia and Africa. In a Y-shaped olfactometer, the essential oil of C.lanceolatus and its main constituent, 1,8-cineol demonstrated 100% and 74% repellency of pluse beetle respectively, at a concentration of 150 µl. At a concentration of 0.1 µl/ml, 100% insect death was achieved using the essential oil and 1,8-cineole. The essential oil was shown to be the most efficient fumigant in terms of oviposition deterrence (96.03%) and antifeedant activity (100%) at a concentrationof 0.1µl/ml. Additionally, when tested on mice, Callistemon lanceolatus essential oil showed encouraging safety profile, with an LD50 of 14,626.3 µl/kg[20]. Biomphalaria alexandrina was susceptible to the molluscicidal effects of the dry powdered C. lanceolatus. A chromogenic bioassay revealed that the C. lanceolatus extract exhibited 80% antithrombin activity[21]. Helicoverpa armigera's development was efficiently suppressed, its larval toxicity was raised, and its normal adult emergence was blocked by extracts from the leaves of Vinca rosea and C.lanceolatus alone and in combination[22].

2.14 Miscellaneous activities:

A study found that by reducing the elevated serum level of enzymes, the methanol extract of C.lanceolatus leaves protected rats' livers against damage caused by carbon tetrachloride (CCl4). Rats with doxorubicin-induced cardiomyopathy responded favourably to an ethanol extract of C.lanceolatus leaves (100mg/kg and 200mg/kg bw). Trichophyton tonsurans, a test dermatophyte, was completely poisonous to the essential oil of C. lanceolatus [7].

3. Recent approaches in novel drug delivery systems:

3.1 Phytosomes for the Treatment of Obesity:

A method of delivering medication or plant extracts made with phospholipids and other solvents is the use of phytosomes[23]. Phytosomes have superior stability profiles in comparison to medication or plant extracts. They also evade degradation of the plant-based ingredient by microbiota and enzymes, enhance permeability of membrane, bioavalibility, optimise chemical efficacy[24]. In order to improve *Callistemon citrinus* leaf extract's absorption and bioavailability while preventing weight gain, study sought to encapsulate it in a phosphatidylcholine complex. Phytosomes of C. citrinus extract were shown good solubility and stability, smaller size, and heigh entrapment capability. A hypercaloric diet was given to male Wistar rats in order to assess the anti-obesogenic activity. For five days, the fresh leaf was macerate at room temperature in a 96% ethanol to water ratio of 1:10. After that, an extract was concentrated at 45°C using a rotating evaporator. There was a 20% yield. The identical concentration of phospholipids and Callistemon citrinus (200 mg/b.w.) was used to create phytosomal complex. This dosage is therapeutically effective in reducing obesity[25][26]and inhibiting oxidative stress[27]. There were 50 mL of hydration in the combination. 1.25 gm of soybean phospholipids and 1.25 gm of Callistemon citrinus extract, 0.72g of Tween 80, 150 mM NaCl, 0.01 M phosphate buffer solution, pH 7.4 and 1% of ethyl acetate were added to the mixture to increase its solubility. The emulsions were made with a VCX 500 ultrasonicator set at 25% amplitude 10 minutes at10°C. The stoichiometric ratio of phytosomes was 1:1. The phytosome complex was kept at room temperature after being put in a glass bottle with an amber tint. To prepare phytosomes, Using the response surface method of central composite design, design expert 11.0.5 was used as an experimental design. Two factors were chosen as independents: rotation speed (rpm) and lecithin concentration (%w/v). Next, how these factors affect the size of the vesicles and the efficacy of entrapment the phytosomes' efficiency was evaluated. Every process was shielded from light. One method for increasing the bioavalibility and solubility of plant extract is the use of phytosomes[28]. In the emulsion, the C. citrinus phytosome average particle size of 129.98 nm±18.30 nm. A substantial amount of entrapment of the leaf extract is shown by its concentration of unbound callistemon citrinus leaves extracts 200mg/kg, which shows a reaction between the leaves extract and soybean phospholipids to create the complex, represents encapsulation efficiency of phytosomes. C. citrinus-loaded phytosomes held their stability for 3.5 months. The phytosomes of Callistemon citrinus were found to be moderately soluble in one solvent and totally soluble in four others. C. citrinus phytosomes, 20% for the first and 10% on the latter, we will assume. The solubility of C. citrinus phytosomes was 90%. Consequently, 80% solubility at last, soybean liposomes are shown by callistemon citrinus extract, both with as well as without tween 80. Interaction between hydrogen bonds,which boosts the chemicals' stability and bioavailability, provides the basis for the creation of phytosomes with plant extract. Thus, compared to bioactive substances, phytosomes have superior lipophilicity and hydrophilicity. Stronger anti-obesity activity was seen in phytosomes loaded with C. Citrinus extract than in the extract itself, this is likely because of the great bioavalibility, which increases the solubility and permits a reduction in dosage C. Citrinus extract and phytosomes exhibited an outstanding capacity to reduce ferric to ferrous as well as a powerful inhibitory effect against the DPPH and ABTS radicals. Due in large part phytosomes' high bioavailability, which boosts their solubility and allows dosage

reduction, the anti-obesity effect of the phytosomes containing C. citrinus extract, is higher than that of the extract alone. The Callistemon citrinus phytosomal formulation exhibited three to four months of stability at20°C, as well as maintaining its main constituents and improving oral bioavailability. C. citrinus phytosomes reduced biochemical and morphometrical features in wistar rat fed a heigh-fat diet, even at low dosages. In addition, the results demonstrated that boosting with Callistemon citrinus phytosomes reduced the animals' excessive weight [28].

3.2 Nanoparticals in Anticancer Activity:

Recent advances have seen significant developments in the field of nanoparticle systems, most notably the use of polymeric nanoparticles for cancer therapy[29]. Since they were made of a range of recyclable and compatible materials, both natural and manufactured, nanoparticles have the potential to be used as carriers for multiple kinds of disorders, particularly cancer[30]. Artificial Materials such as PVA, PLA, and PLGA are ideal for creating polymeric nanoparticles as they are polymers or copolymers. Encapsulating bioactive chemicals and delivering them to targeted sites through nanoparticle delivery systems has proven to be an effective way to improve their absorption and/or bioavailability[3132]. Applying advancement in nanotechnology, phenols from Citrus citrinus extract were encapsulated. The stability and efficacy of the nanoencapsulated Citrus citrinus nanoparticles were examined the effects on growth and development of three types of breast cancer cell lines was assessed. The mature plants of the bottlebrush (Callistemon citrinus), grown in Pakistan's Punjab Province's Chakwal District, were collected for their leaves and stems. After being freeze-dried at -70°C, fresh tissue was triturated. After homogenising sample of 20g of freez dried tissue containing 200ml methanol, homogenate put in orbital shaker for a whole day. A Whatman (#4) filter paper used to filter the mixture, and a rotary evaporator was used to concentrate the filtrate. For every test, new extracts were made. An approach called nanoprecipitation was used to create the nanoparticles[33]. When 50 mg of PLGA produced in acetone solution was mixed with 5.0ml of methanolic tissue extract agitated at150rpm for 45mintes, an organic phase was formed. After dissolve 1g of polyvinyl alcohol (PVA) in 100ml of pure H2O, PVA was heated and agitated to dissolve it, creating aq. phase of 1% polyvinyl alcohol solution. Drop by drop, orgnic portion of PLGA tissue extract added to 20 mL polyvinyl alcohol solution. A no-precipitation method was used to create PLGA nanoparticles. When C. citrinus was nanoencapsulated inPLGA nanoparticals, it increased its effect in contradiction of the breast cancer cell lines. Furthermore, cytotoxic activity of C. citrinus extracts in both free and encapsulated forms was further enhanced by the addition of berberine.

3.3 In vitro Silver and Gold Nanoparticals in Antioxidant, Antimicrobial and Cytotoxic Activities:

There are a number of studies in application of herbs in synthesis of nanoparticles, particularly gold AuNPs or silver AgNPs. 150 g of dry powdered Callistemon citrinus leaves were immersed into 1500ml of 85% methanol for week at room temperature, stirring daily. The leaves were then filtered and extracted four more times. The rotatory evaporator was used to extract the organic solvent in vacuum. The 50 g of 85% methanol extract defatted by petroleum ether at 60–80 °C. Using organic solvents such as CH2Cl2, EtOAc, and n-BuOH, 45 grams of the defatted methanol extract were fractionated (3 x 100 ml for each solvent) Silver nanoparticle (AgNP) biosynthesis Due to its numerous applications, silver, a fairly popular and well-known metal, has increased in value. Silver nanoparticles are one type of nanoparticle that has several important uses, particularly in the biomedical industry[3435]. In the present investigation, the addition of Callistemon citrinus leaves extract to an aq. solution of silver nitrate (5mM) resulted in a brownish color shift as a result of reduction of silver ions into metallic silver. Generated solution UV-vis absorbance was measured, and a peak was observed to occur at roughly 450 nm. Silver nanoparticles (AgNPs) were synthesized environmentally employing The colour of Roheda aqueous extract at 60 °C change into pale yellow to light brownish solution. Synthesized nanoparticles UV-vis analysis showed that the particles' sizes ranged from 5.85 nm to 77.48 nm, indicating the formation of AgNPs. Microscope shows the particle's size varies between 3 and 18 nm. Colour of the reaction mixture change to dark brown after 20 minutes at room temperature synthsis of silver nanoparticals by Annona reticulata, seen that creation of AgNPs. Sperical silver nanoparticals with distance about 10nm were synthesized using the extract of sacred leaves our findings showed that the development of AgNPs was indicated by a colour shift from colorless to yellowish brown to raddish brown to colloidal brown. Due to surface plasma resonance, the generated AgNPs' UV/vis maximum has been found to be between 425 and 475 nm in wavelength. Using C. citrinus leaf extract, silver nanoparticles with diameters between 8 and 14 nm were synthesised, and their microstructure was examined using transmission electron microscopy. metallic Ag's distinctive peaks at 37.8°, 43.3°, and 63.5°, which match the crystallographic The silver phases with (1 1 1), (0 0 2) and (0 2 2) respectively, define property of crystalline metallic silver phase. For Ag, the crystalline size was determined to be approximetaly 20nm based on the line width of the peak from the crystalline plane (1 1 1). The synthesis of metallic silver (in nano state) and its purity have been investigated in a number of studies using XRD of plant leaves extract biosynthesizes silver nanoparticals[35]. Gold nanoparticle biosynthesis (AuNPs). The surface plasma resonance phenomena caused a alteration in color from yellow to purple. When callistemon citrinus leaves extract were introduced to gold salt (HAuCl4). Shimadzu 2401PC spectrophotometric measurements UV-Vis show that generated nanogold solution maximum absorbance was at 535 nm. Gold nanoparticles (AuNPs) were biologically synthesised using extract from Eclipta prostate leaf; the resultant AuNPs had a maximum spectral absorbance at 534 nm and a ruby-red hue[36]. Additionally, when Au ions were treated with an aq. Extract of Elettaria cardamonum (ELAICHI), a violet colour was produced as a visible indication of the creation of Au metal.Our findings further demonstrated that, ratio of Au solution with extract, the generated AuNPs exhibited maximum absorbance at 540, 550, and 540 nm. According to measurements made using transmission electron microscopy, the average size of the synthesised AuNPs was 5.8 to 8.84 nm. The metallic Au phase is assigned to Au-NPs obtained in the presence of AuCL4-analogous diffraction peaks, with the characteristic peaks at 38.4, 44.5 and 64.3 assigned to the crystallographic planes (1 1 1), (2 0 0) and (2 2 0). The structural properties of Au-NPs was studied using the XRD technique. The existence and purity of AuNPs have been assessed by a number of XRD investigations. Triangular gold nanoparticles (AuNPs) were biosynthesised using an Aloe vera leaf extract. Using leaves from Cinnamomum camphora and Emblica officinalis, Reported synthesising gold nanoparticles with sizes of 55-80nm and 15-25nm in that order, and spherical and trilateral forms. The leaf of callistemon citrinus can be used to make silver and gold nanoparticles. The synthetic AgNps and AuNPs have diameters ranging from 8–14 nm and 5.8–8.84 nm, respectively, according to the TEM study. Additionally, the majority of C. citrinus extracts examined demonstrated potent antioxidant activity both qualitatively and quantitatively. In addition, these fractions demonstrated potent in vitro antibacterial activity against four types of pathogenic microorganisms: Candida albicans, MRSA,

Pseudomonas aeruginosa, and Staphylococcus aureus. Moreover, the cytotoxic outcomes revealed that the LC50 values varied, ranging from 63.09 to 501.18 µg/ml. It sheds a spotlight on the potential uses for C. citrinus leaves as a natural source of cytotoxic, antioxidant, and antibacterial compounds[37].

3.4 Gold Nanoparticals in Antimicrobial, Antitriypanocidal and Antimalarial:

Plant extracts are increasingly being used in the biogenesis of gold nanoparticles because of their potent antibacterial properties. The procedure is simple, Because of their extremely small size, solubility, tunable optical, non-cytotoxic, appreciative uppermost layer, physical and chemical properties also general presentation in through drug delivery, imaging, analysis and curative purposes, gold nanoparticales have revolutionized the field of medicine[3839]. The fresh C. citrinus seed was allowed to air dry for approximately 4 weeks at normal temperature. The dry seeds were crushed up by automatic mixer (PXMFC 90D). 30g ground sample with 250ml of water were mixed and for a whole day, the mixture was agitated at 200 rpm using an orbital shaker. The resulting filtrate was then dried powder after being lyophilized and stored in a covered until the amount of time needed for the synthesis of nanoparticles, centrifuge the tube at 4°C. In order to create gold nanoparticles, the plant extract (12.5 mL) was added to90 mL of Gold (III) Chloride solution (0.001M). The mixture was then continuously stirred 6hr while the process was conducted in the shady room to avoid unneeded photochemical responses. Following a 6-hour incubation period, the mixture was centrifuged for 15 minutes at 15,000 rpm at room temperature. The tablet that was produced after this procedure remained air dried and twice washed with purified H2O; resulting silver nanoparticles were employed in the various experiments that follow. It was successful to synthesize AuNPs from C.citrinus seed extract. It was tested against several bacterial strains and trypanosome and plasmodia parasites. The majority of the synthesized nanoparticles had irregular spherical shapes, according to SEM analysis, and TEM analysis revealed normal dimension of roughly 37nm. Interestingly, it was discovered that the synthesized AuNPs remained non cytotoxic to HeLa cells and could prevent entire infectious straining tested, authorizing plant's use as a great source of certainly taking place cytotoxic, antimicrobial medications. However, it was not effective against plasmodia and trypanosome parasites[40].

3.5 Silver Nanoparticles for Evaluation of Antibacterial Activity:

Silver Nanoparticals synthesis by plant-mediated means is a quick, easy, safe, and environmentally beneficial process. With no harmful effects on human cells, silver nanoparticles have considerable bactericidal activity at the quantities they are used in. Their synergistic effects also significantly boost antibacterial activity of traditional antibiotic beside bacteria those confrontation to several medicine. In this work, silver ions in silver nitrate solution were reduced using an aqueous extract of Callistemon citrinus. The following study examined the antibacterial activity of nanoparticles produced using a range of qualitative and quantitative techniques against Salmonella typhi, Listeria innocua, Escherichia coli, Staphylococcus aureus. In order toward create silver nanoparticles; 5ml leaf extract in concentration of 100 mg/ml were combined with 25 mL of silver nitrate solution, which was then kept at 20 °C for 24 hours. The solution will turn red, which indicates that silver nanoparticles are being produced there. The spectrophotometer-produced absorption spectra of the silver nanoparticles were made in order to stabilise their presence. Silver nanoparticles were synthesised using C. citrinus leaf aqueous extract, and their antibacterial activity was evaluated using disc diffusion agar, minimal inhibitory concentration, and well diffusion agar (microdilution broth). The minimal concentration of bactericidal medications that can eradicate Salmonella typhi, Listeria innocuous, Pseudomonas aeruginosa, S.aureus and E.coli. The diameter inhibitory region increased as the concentration of silver nanoparticles increased, as determined by the disc diffusion agar method. The most significant impact of silver nanoparticles synthesised with an aqueous extract of C. citrinus leaves dosage of 150mg/ml were observed in Pseudomonas aeruginosa. For every pathogenic bacterium under investigation, an inhibitory zone was seen at every concentration. The results indicate that not all pathogenic bacteria were suppressed by 18.75 mg/ml of nano silver particles in the well diffusion agar method. No major variance were create in any of amounts of silver nanoparticles synthesised for the bacteria Salmonella typhi, a strain of Staphylococcus aureus, and E. coli, according to the statistical analysis. Escherichia coli, Staphylococcus aureus, Listeria innocua, P. aeruginosa, and Salmonella typhimurium all had MICs of 128, 256, 256, 256, and 512 mg/mm, in that order. Every pathogenic strain had an MBC of 512 mg/mm. The study's findings demonstrated that Callistemon citrinus leaf extract possesses a good capacity for silver nanoparticle synthesis. Callistemon citrinus leaf extract was used to create nanoparticles, which exhibited strong antibacterial action against tested pathogenic microorganisms, particularly Gram-negative bacteria. Although more in vitro study is required, Nanoparticles made using green synthesis can be employed as an antibacterial agent to fight infectious illnesses due by multiple microbiological strains[41].

3.6 Silver Oxide Nanoparticals of Callistemon Citrinus Therapotic Potential:

The use of nanoparticles in molecular biology has grown in popularity, particularly when it comes to serving as scaffolds for different biological molecules like proteins, DNA, RNA, and antibodies. In addition, dual-layered and protein-shelled nanoparticles have been developed for a range of uses in electronics and medicine. Silver oxide is well-known for its capacity to function as a chemical sensor for a variety of substances, including carbon monoxide and ammonia. It is also known to catalyse ethylene and methanol oxidation processes. Silver oxide nanoparticles have good optical and fluorescent properties[4243]. Herbal extracts are currently being used extensively in nanoparticle synthesis due to their cost-effectiveness and ability to produce more stable nanoparticles than other approaches. Thus, Callistemon lanceolatus D.C. is employed in this work to synthesise silver oxide nanoparticles. Commonly referred to as the bottle-brush tree, C. lanceolatus is an ornamental shrub in the Myrtaceae family. Its recognised contents include triterpenoids , polyphenols , and various volatile oils . These compounds may be the cause of its therapeutic qualities. Therefore, we have shown in this study that silver oxide nanoparticles may be biologically synthesised utilising the aqueous extract of C. lanceolatus, and we have also described their substantial cytotoxic and antioxidant properties. In order to create silver oxide nanoparticles, 5 ml of recently made aqueous C. lanceolatus leaf extract was added to an Erlenmeyer flask along with 100 ml of a 1 mM AgNO3 solution. To stabilise the nanoparticles, a milligramme of sodium dodecyl sulphate (SDS) was introduced. A shaking incubator with dark conditions was used to incubate the setup at 37 C in mandate to bounds the photo activation of silver nitrate. Under identical circumstances, a control setup with just 1 mM silver nitrate solution was also kept up to date. UV-visible spectroscopy was used to track the synthesis, and absorption data were recorded on a regular basis to determine how long it needed for the reaction to take place. An Erlenmeyer flask was filled

with 100 ml of a 1 mM AgNO3 solution and 5 ml of freshly prepared aqueous C. lanceolatus leaf extract in order to produce silver oxide nanoparticles. One milligrams of sodium dodecyl sulphate (SDS) was added to the nanoparticles to stabilize them. To minimize the photo activation of silver nitrate, the setup were hatched at 37 C in a shaking incubator under dark circumstances. A control setup using only 1 mM silver nitrate solution was also maintained current under the same conditions. UV-visible spectroscopy was employed to monitor the synthesis, and regular recording of absorption data was done to ascertain the reaction's half-life. The first account of C. lanceolatus's biosynthesis of Ag2O nanoparticles. New method for producing silver oxide nanoparticles through the use of an aqueous C. lanceolatus leaf extract. The oval or hexagon-shaped biologically synthesised nanoparticles have a size of 330 nm. In addition, the compounds exhibited significant antioxidant and cytotoxic capabilities in multiple in vitro experiments, indicating their potential medicinal uses across optoelectronic and storage device applications. Thus, it is possible to draw the conclusion that this work describes a brand-new, quick, affordable, and environmentally safe process for creating biologically active silver oxide nanoparticles[44].

Conclusion:

Recent approaches in novel drug delivery systems for callistemon citirnus showing advantages for enhancing the therapeutic potential of this plant. Through innovative delivery methods such as nanoformulations and targeted delivery systems,the bioactive compounds present in callistemon citrinus can be more effectively delivered, leading to improved efficacy and reduced side effects. The effectiveness of callistemon citrinus extract as a therapeutic agent has been demonstrated through various studies indicate that the extract possesses potent antioxidant, antimicrobial, anti-inflammatroy and antifungal things, creating it a hopeful applicant on behalf of a extensive variety of health presentations, the integration of Callistemon citirnus extract into novel drug delivery systems holds immense promise for advancing personalized medicine, improving treatment outcomes and addressing global healthcare challenges in a sustainable and accessible manner. Challenges exist in the development and application of novel drug delivery systems for extract, there are ample opportunities for innovation,collaboration and advancement in the field, ultimately contributing to improved healthcare outcomes and patient care potentially leading to more effective treatments in the future.

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Conflict of interest:

The author declares that there are no conflicts of interests.

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