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Aldoses reductase and protein glycation inhibitory activity of papaya leaf and green tea mediated Silver nanoparticles

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Abstract:

Introduction: Aldose reductase is the rate-limiting enzyme of the polyol pathway. AR catalyzes the conversion of glucose to sorbitol and further converts sorbitol into fructose. AR inhibitors are involved in the pathophysiology of diabetic complications, including cataracts.Glycation is a nonenzymatic browning reaction caused by an amino-carbonyl reaction between a reducing sugar and an amino group of a protein or lipid. The nonenzymatic reaction leads to chemical modifications of tissue proteins, called advanced glycation end products, resulting in functional disturbances of the proteins.Carica papaya also simply known as papaya or pawpaw,Papaya leaf contains unique plant compounds that have demonstrated broad pharmacological potential in test-tube and animal studies.
Aim: Aldoses reductase and protein glycation inhibitory activity of papaya leaf and green tea mediated Ag NPS
Materials and methods: Advanced Glycation end product (AGE) assay
1 mg/mL bovine serum albumin in 50mM sodium phosphate buffer (pH 7.4) and 0.02% sodium benzoate into 0.2M fructose and 0.2M glucose. The reaction mixture (2.75mL) was treated with different volumes PL-GT-Ag nanoparticles. Amino guanidine was used as positive control. After incubating at 37°C for 3 days, the fluorescence intensity of the reaction was determined at 350 nm and 450 nm, using Biotek synergy multi-mode reader. The percentage activity was calculated with respect to solvent control. Determination of Aldose Reductase Inhibition
A total of 531µL of 0.1 M potassium buffer (pH 7.0), 90µL of NADPH solution , 90µL of recombinant human aldose reductase (6.5U/mg) , 90µL of ammonium sulfate solution, and 90 µL of DL-glyceraldehyde were mixed with 9µL of different concentrations of PL-GT-Ag nanoparticles in a cuvette, and the activity of AR was assessed spectrophotometrically by measuring the decrease in NADPH absorbance at 340 nm for 3 min using a spectrophotometer
Result and discussion:The synthesis of silver nanoparticles using plant extracts is used in anti-parasitic, anti-malarial, bactericidal, fungicidal, and antiviral activity.the formation of AgNPs was confirmed by observing the color change of the reaction mixture. Within 15 min of the exposure of the C. papaya extract, the color of silver nitrate (AgNO3) solution changed from transparent to a dark brown color which is a primary indication of AgNPs production. The presence of different compounds in the extract has shown that the plant leaves possess high potential aldose reductase inhibition

Conclusion: In this study, a simple, biological and low-cost approach was done for the preparation of Silver nanoparticles using papaya leaf and green tea extract. Thus papaya leaf and green tea mediated silver nanoparticles can be subjected to the various other biological activities such as antibacterial, antifungal, cytotoxic evaluation to know the efficiency of these nanoparticles.

Keywords: *Carica papaya*, silver nanoparticles

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Introduction:

Nanomedicine is an emerging field expanding rapidly because of the development and incorporation of new nanocomposites into a range of products and technologies.(1) In recent years, the application of nanoparticles (NPs) in medicine has increased and expanded to the fields of molecular imaging, drug delivery, diagnosis and treatment of cardiovascular diseases, wound healing and development of materials and medical devices with antimicrobial properties.(2)

New applications of NPs and nanomaterials are emerging rapidly in biomedical sciences . This decade has witnessed the inception of new significant technological products particularly based on nanotechnology, NPs synthesis is being widely explored since they exhibit unique size and shape dependent properties for applications in optics, electronics, catalytic systems, magnetic and biomedical fields such as HIV inhibition, cancer cell cytotoxicity and genotoxicity.(3) Apart from this, recently the anti-tumour effect of AgNPs has been reported against different cancerous cell lines. NPs with the size range between 1 and 1000 nm are mainly explored for the diagnosis and treatment of human cancers, which led to the new discipline of nano-oncology(4).(3,4)

There are a number of methods used for the synthesis of silver nanoparticles (AgNPs) including physical and chemical methods, electrochemical reduction, photochemical reduction and thermal evaporation. (5)However, a rapid and green synthesis method using plant extract has developed an enormous interest in AgNPs synthesis due to the green chemistry approach. Moreover, it is simple, cost-effective, eco-friendly, easily scaled up for large-scale synthesis, without using toxic and redundant chemicals in solid, liquid and gaseous form.(6) Indeed, a number of bacteria, fungi and yeast have been well-known for the synthesis of non-toxic noble NPs. However, the microbial-mediated synthesis of NPs is not industrially feasible as it requires expensive medium and maintenance of highly aseptic conditions.(7)

In this context, plant-mediated NPs synthesis seems to be a cost-effective as well as eco-friendly method. Moreover, NP synthesis from plants with medicinal properties proves to be beneficial in treating various ailments in a better and easy way.(8) On such plant is Papaya, a tropical fruit, often seen in orange-red, yellow-green and yellow-orange hues with a rich orange pulp. Whole plant parts, fruits, roots, bark, peel, seeds and pulp are known to have medicinal properties.(9) It has been used for the treatment of numerous diseases like warts, corns, sinuses, eczema, cutaneous tubercles, blood pressure, dyspepsia, constipation, amenorrhea, general debility, expel threadworms and stimulate reproductive organs. It also effectively treats and improves all types of digestive and abdominal disorders. Leaves of papaya, one of the plant parts with numerous medicinal value, have the history of streaming and eating with spinach in Asia.(10) It has been found to have a significant effect on various tumor cell lines and the tea extract of leaves found to have antimicrobial properties, ease menstrual pain, relieve nausea, increase the appetite and antispasmodic activities.(11) Phytochemical investigations were carried out on this plant by several authors, which revealed the presence of carbohydrates, phenols, flavonoids, sterols, alkaloids, saponins, cardiac glycosides, ecdysterone *etc*., from different parts of this plant. Survey of the literature revealed that NPs synthesis from *Carica papaya* leaves is scanty. In view of this, the present study was designed to biosynthesize NPs from leaves to study the reducing Ag+ions and stabilizing the particles and confirm AgNP synthesis by using various spectroscopy and microscopic methods.(12)

Materials and Methods

Advanced Glycation end product (AGE) assay

Advanced glycation end products (AGEs) are formed by non-enzymatic glycosylation of proteins that enhance vascular permeability in both micro and macro vascular structures by binding to specific macrophage receptors. The PP-Sr nanoparticles were evaluated for its activity on AGEs formation. AGE reaction mixture was constituted as follows; 1 mg/mL bovine serum albumin in 50mM sodium phosphate buffer (pH 7.4) and 0.02% sodium benzoate into 0.2M fructose and 0.2M glucose. The reaction mixture (2.75mL) was treated with different volumes PL-GT-Ag nanoparticles (5, 10, 20, 40, 80 & 160µL). Amino guanidine was used as positive control. After incubating at 37°C for 3 days, the fluorescence intensity of the reaction was determined at excitation and emission wavelengths of 350 nm and 450 nm, respectively, using Biotek synergy multi-mode reader, USA. The percentage activity was calculated with respect to solvent control.

Determination of Aldose Reductase Inhibition

A total of 531µL of 0.1 M potassium buffer (pH 7.0), 90µL of NADPH solution (1.6 mM in potassium buffer), 90µL of recombinant human aldolase reductase (AR) (6.5U/mg) (Sigma, USA - SRP6371-100UG), 90µL of ammonium sulphate solution (4 M in potassium buffer), and 90 µL of DL-glyceraldehyde (25 mM in potassium buffer) were mixed with 9µL of different concentrations of PL-GT-Ag nanoparticles (5, 10, 20, 40, 80 & 160µL) in a cuvette, and the activity of AR was assessed spectrophotometrically by measuring the decrease in NADPH absorbance at 340 nm for 3 min using

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a spectrophotometer (Biotek Synergy H4 multimode reader, USA). Quercetin was used as positive controls. The inhibition of AR (%) was calculated using the following equation: (1 − (△A sample/min) – (△A blank/min)/(△A control/min) − (△A blank/min)) × 100%, where △A sample/min is the decrease in absorbance over 3 min with reaction solution, test sample, and substrate, and △A control/min without the test sample.

Results:

The synthesis of silver nanoparticles using plant extracts is used in anti-parasitic, anti-malarial, bactericidal, fungicidal, and anti-viral activity.he formation of AgNPs was confirmed by observing the color change of the reaction mixture. Within 15 min of the exposure of the C. papaya extract, the color of silver nitrate (AgNO3) solution changed from transparent to a dark brown color which is a primary indication of AgNPs production. The presence of different compounds in the extract has shown that the plant leaves possess high potential aldose reductase inhibition

Figure 1:

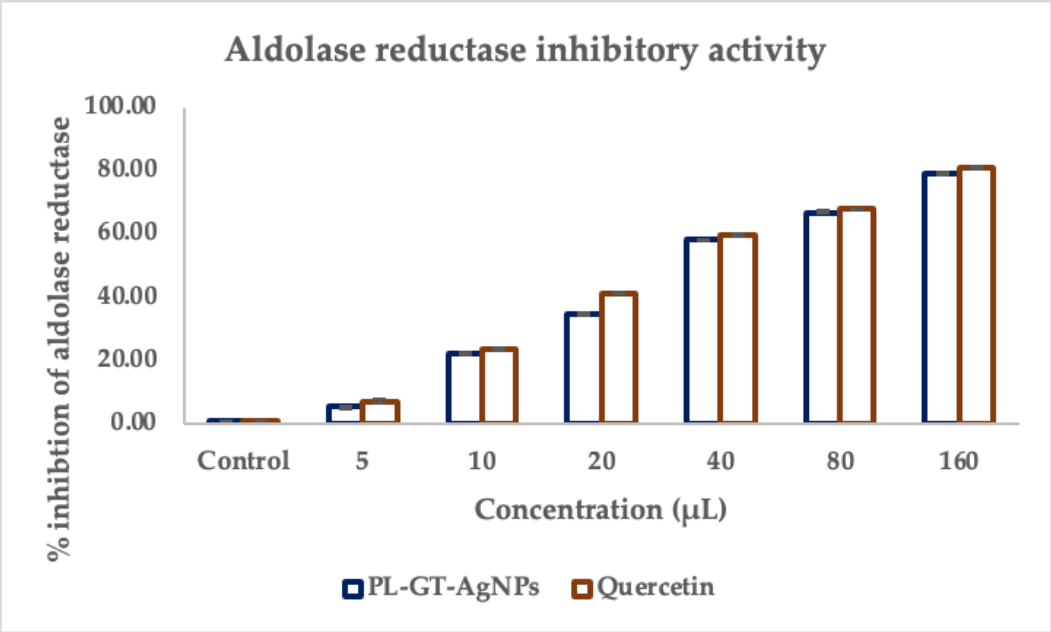
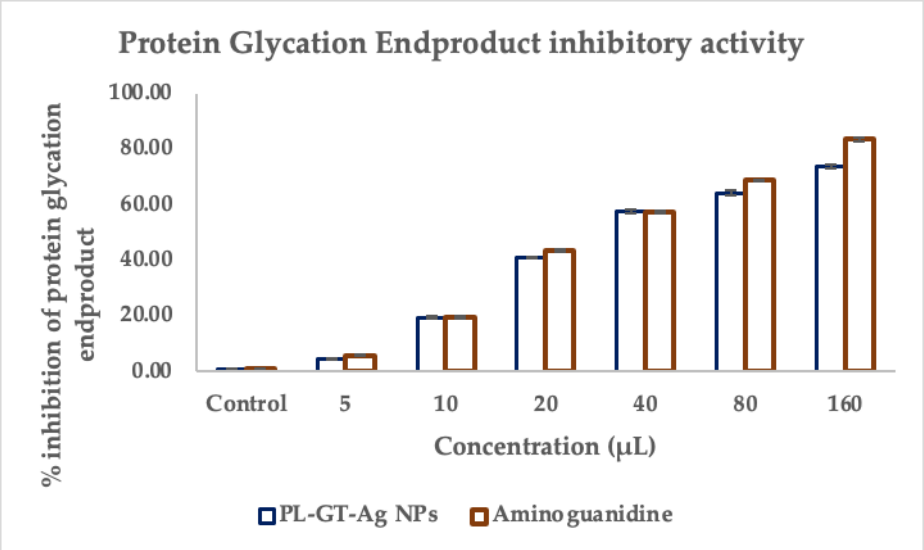


Figure 2:



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Discussion :

The synthesis of silver nanoparticles using plant extracts is getting more attention, due to their application in biomedical sciences such as anti-parasitic, anti-malarial, bactericidal, fungicidal, and antiviral activity(10) . In this study, the AgNPs were synthesized using aqueous and methanol extracts of *C. papaya*. Initially, the formation of AgNPs was confirmed by observing the color change of the reaction mixture.(11) Within 15 min of the exposure of the *C. papaya* extract, the color of silver nitrate (AgNO3) solution changed from transparent to a dark brown color which is a primary indication of AgNPs production.(12) This color change was observed due to the reduction of Ag+ ions in the solution of AgNO3 into AgNPs. The color change was in line with previous studies that demonstrated the appearance of a brown color, due to excitation of surface plasmon vibrations with the synthesized AgNPs .(13) Furthermore, the production of AgNPs was confirmed by UV-Visible spectroscopic analysis, which quantifies the absorption spectra. The UV-visible spectrometry showed a sharp peak at 450 nm, confirming the formation of silver nanoparticles. (14)This is in range with previously reported studies on the synthesis of AgNPs from *C. The gas chromatography–mass spectrometry analysis of previous studies states that the leaves of C. papaya possess phenolic compounds such as quercetin, protocatechuic acid, 5,7 dimethoxycoumarin, chlorogenic acid, and kaempferol [35] used in our in silico study.(15) This study revealed possible interactions between the various bioactive compounds present in the C. papaya leaf extract and both the N- and C-terminal domains of the viral NS-5 protein. The NS-5 protein N-terminal domain possesses the Cap-0 specific (nucleoside-2'-O-)-methyltransferase, which catalyzes the methylation of Cap-0 at the 2'-hydroxyl of the ribose of the first nucleotide, using S-adenosyl-L-methionine as the methyl donor. (16)This reaction is the last step in mRNA capping, the creation of the stabilizing five-prime cap on mRNA. The C-terminal domain is the Flavivirus RNA-directed RNA polymerase, which produces a polyprotein from the ssRNA genome. Thus, the viral inhibition observed via the focus reduction neutralization test could be due to the inhibition of viral replication.(17)*

The present study was aimed to identify the phytocompounds present in *Carica papaya* and to synthesize AgNPs from the aqueous extract of *Carica papaya* leaves which is distributed as a weed throughout India. (18)Phytochemical study of *Carica papaya* leaf extract shows the positive results for carbohydrates, tannins, saponins, phenols, flavonoids, alkaloids, anthocyanin, terpenoids and triterpenoids.(18,19) On the other hand coumarins and steroids were absent in the aqueous extract.The bioactive compounds such as polyphenol, carbohydrates, vitamin and trace elements present in the leaf extract plays an important role as an antioxidant, anticancer, antitumor, anti-inflammatory, anti-obesity, anti-helminthic, analgesic, antipyretic, anti-nociceptive, anti-hepatitis, hepatoprotective, cardiac, Diuretic agent, attributing platelet augmentation, anticancer property, anti-acne activity, easing menstrual pain and relieving nausea.(20)

Conclusion: In this study, a simple, biological and low-cost approach was done for the preparation of Silver nanoparticles using papaya leaf and green tea extract. Thus papaya leaf and green tea mediated silver nanoparticles can be subjected to the various other biological activities such as antibacterial, antifungal, cytotoxic evaluation to know the efficiency of these nanoparticles.

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