



Enhancement of antidiabetic activity of curcumin rhizome extract using silver nanoparticles

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Abstract

Objective: In this current work, for enhancing the effect of the antidiabetic potential of curcumin extracted from *Curcuma longa* Linn by encapsulating the extract of curcumin in silver nanoparticles was aimed.

Methods: Curcumin was extracted from *Curcuma longa* by Soxhlet method. Curcumin shows poor solubility and low absorption rate therefore its silver nanoparticles was formed to increase solubility, absorption as well as affectivity against diabetes. Various analytical methods and assay such as particle size, zeta potential and fourier transform infrared spectroscopy (FTIR), drug release and *in vitro* antidiabetic study on streptozotocin induced diabetic rats were employed for monitoring the formation of curcumin extract encapsulated silver nanoparticles.

Results: Presence of silver nanoparticles with an average size of 26.78 nm was revealed by particle size analyzer and zeta potential may obtain -4.68 mV. CSNPs (curcumin extract encapsulated silver nanoparticles) were able to release 94.35% curcumin in 12 hrs whereas the plain curcumin extract was released 95.68% in 8 hrs.

Conclusion: The conclusion after the result obtained by *in vitro* antidiabetic activity, demonstrated that CSNPs inhibit the blood glucose level than plain curcumin. This work shows that curcumin rhizome extract encapsulated silver nanoparticles shows potential antidiabetic activity.

Keywords: Antidiabetic Activity, Fourier Transform Infra-Red Spectroscopy, Particle Size, Curcumin, Silver Nanoparticles

Nanoparticles can be defined as the formation, development, enhancement and exploration of nano sized materials having size range of (1-100 nm). Now a day's nanotechnology works on the design and development of many novel formulations for the prevention, treatment and diagnosis of many critical diseases [1], like cancer, diabetes, T.B. and cardiovascular diseases etc. Because of their specific characteristics, silver nanoparticles (AgNPs) may used as catalysts [1], in spectrally selective coatings for absorption of solar energy as optical sensors in fabric tailoring as well as in electronics devices and in various therapeutic activity of bactericidal agents [2]. AgNPs prepared by green synthesis phenomena is effective in biological environmental systems [3].

The spice turmeric, which is derived from the root of the plant *Curcuma longa*, has been described as a treatment for diabetes in Ayurvedic and traditional Chinese medicine for thousands of years. The most active component of turmeric, curcumin, has caught scientific attention as a potential therapeutic agent in experimental diabetes and for the treatment of the complications of diabetes patients primarily because it is effective in reducing glycemia and hyperlipidemia in rodent models and is relatively inexpensive and safe [4]. Srinivasan in 1972 observed that the inhibitory effect of curcumin in the blood glucose level [5].

Curcuma longa were collected from Botanical garden, Guru Ramdas Khalsa Institute of Science and Technology (Pharmacy), Jabalpur, MP, India. AgNO₃ and ethanol and other chemicals were purchased from Chemical drug house, New Delhi, India and other chemical used analytical reagent grade.

Curcuma longa (turmeric) was and cleaned using deionized water and then rhizomes were scrapped. It was dried in pollution free atmosphere at room temperature. After few days it was powdered using mixer grinder. 20 g of the turmeric powder was taken into a thimble and placed in a Soxhlet apparatus, with ethanol as a solvent. Finally dark yellow extraction was obtained and filtered. The filtrate was kept in Ultrasonicator at 20 KHz frequency for about 20 min to reduce the particle size of the curcumin.

A 0.017 gm of silver nitrate was accurately weighed and dissolved in 100 ml of double distilled water and stored in amber coloured bottle until further use. A 100 ml of 1 mM silver nitrate (AgNO₃) was heated to boiling. To this appropriate solution, 10 ml of curcumin extract was poured for reduction of silver ions (Ag⁺), then kept at room temperature for 1 h, the change in colour of solution was examined timely. The color change from yellow to yellowish brown indicated the formation of silver nanoparticle. It observed that the

aqueous silver ions could be reduced by the ethanolic extract of curcumin to generate very stable silver nanoparticles. The prepared silver nanoparticles name as CSNPs was lyophilized for further use [6].

FTIR Spectra of CSNPs was determined with a FT-IR spectrophotometer (Cary- 630 FTIR, Agilent Technologies). The particle size and zeta potential of CSNPs was determined using particle size analysis instrument (Malvern Instrument, United Kingdom).

Drug release study was also performed by dialysis tube method by using dialysis tube (MWCO 2000 Da) in PBS (pH 7.4) rpm at 37 ± 2 °C and then the samples were examined by using HPLC.

Wistar albino rats weighing about 150-200 gms of either sex were taken for the pharmacological studies (antidiabetic activity). The experimental protocol was approved Institutional Animal Ethics Committee of the Guru Ramdas Khalsa Institute of Science and Technology (Pharmacy), Jabalpur (MP) India (Registration Number 1471/PO/a/11/CPCSEA, India). The animals were kept under standard conditions, room temperature (25 °C), 45-65% relative humidity, standard pellet diet and water was provided. The animals were housed for one week in cages prior to the experiments to make them to laboratory conditions. Animals were divided into four groups having eight rats in each group. Group first serves as control, Group second serves as standard and treated with metformin hydrochloride (10 mg/kg of body weight) and group third serves as test and treated with CSNPs (200 mg/kg of body weight) and group four treated with plain curcumin.

The acclimatized animals were kept fasting for one day with water ad libitum and injected intraperitoneally at a dose of 150 mg/kg of body weight of streptozotocin freshly prepared in normal saline (0.9% w/v) solution. Before starting the experiment animals were grouped according to their weight of body. After 60 min of streptozotocin administration, animals were given feed according to their need and provided 1 ml of (100 mg/dL) glucose i.p to battle encountering severe hypo glycaemia. After 72 hrs of streptozotocin injection, the animals were examined for presence of diabetes by estimating their blood glucose level by using glucometer. The blood glucose levels were more than 140 mg/dl was criteria for diabetes according to world health organization. To the animals the CSNPs (200 mg/kg of body weight, intra peritoneally) and standard drug metformin hydrochloride (10 mg/kg body weight) were administered by dissolving in 2% Tween 80, water and normal saline respectively. The blood glucose levels were monitored at interval of initial (zero hour), 1st, 3rd, 5th and 7th day of administration of unit dose for acute and controlled release action was studied respectively. The body weight of the animals from all the groups was recorded and all the parameters were tabulated [7, 8].

FTIR analysis was done to measure the characterization and

conjugation of potent biomolecules of curcumin with silver nanoparticles. According to the FTIR spectra of CSNPs different peaks was obtained which indicates different functional groups and intermolecular bonding of CSNPs. The spectra are obtained at 682, 972, 1081, 1178, 1309, 1443, 1555 and 1686 cm^{-1} indicates the presence of aromatic C-H bending, N-H stretch and O-H carboxylic acid, C-O-C stretch, C-N stretching of aromatic amine group and C-N stretching ester and ethers in the residual solution and NO_3^- group, C=C bonding, =C-H stretch respectively. The variety of functional groups indicated in FTIR spectra are mainly obtained from heterocyclic substances that are generally water soluble compounds of curcumin. So it can be understood that various water soluble heterocyclic compounds like alkaloids and flavonoids works as the capping ligands for the formation of CSNPs.

The average particle size of CSNPs were found to be 26.78 nm and distribution of particles size of CSNPs were found to be 72.65% of 29.31 nm, 15.3% of 26.1 nm and 12.05% of 24.5 nm and zeta potential of CSNPs was found to be -4.68 mV.

The release of curcumin from the CSNPs demonstrated that the AgNPs have sustained release property. The conclusions established the fact that there was a prominent time prolongation of curcumin release from CSNPs system. CSNPs were able to release 94.35% curcumin in 12 hrs whereas the plain curcumin was released 95.68% in 8 hrs.

The data of the blood glucose level of rats treated with streptozotocin (150 mg/kg body weight) produced diabetes within 72 hrs. After 72 hrs of streptozotocin administered the blood glucose levels of rats were observed above 150 mg/dl. (Table 1) According to the world health organization the blood glucose level above 150 mg/dl indicates the hyperglycaemic action. Extreme thirst, downfall in body weight were also noticed (Table 2). The administration of curcumin ethanolic extract at a dose of 200 mg/kg body weight showed significant antihyperglycaemic effect which was evident from the 1st day. The reduction in blood glucose was highly significant on the 7th day. The antihyperglycaemic effect of the extract on the fasting blood sugar levels on diabetic rats is shown in Table 1, the fasting blood sugar level of diabetic animal notabaly reduced from 234 ± 1.11 mg/dl to 82 ± 0.5 mg/dl on 7th day after the administration of the CSNPs. The decreasing blood glucose levels are comparable to that of 10 mg/kg of metformin hydrochloride. Thus streptozotocin proved to be a suitable compound for inducing experimental diabetes with specific symptoms such as given above. Watching the complications associated with marketed antidiabetic drugs, health care personnels are searching for safe alternatives for them. The blood glucose levels of the hypoglycaemic activity of streptozotocin induced diabetic rats and effect of CSNPs on diabetic rats were given in Table 1

and 2 respectively. It shows the reduction in blood glucose levels and effect on body weight. Based on our recent results, it looks like that ethanolic extract of curcumin shows notable blood glucose lowering in streptozotocin induced diabetic rats. Further studies are necessary to find the exact mode of action of the hypoglycaemic activity of CSNPs.

In the present study we observed that curcumin extracted from *Curcuma longa* rhizome may be good source for the synthesis of AgNPs and this approach for synthesis of AgNPs of ethanolic extract of *Curcuma longa* has many advantages

including the ease with which the process can be scaled up and its economic viability with use of such eco-friendly nanoparticles as an antidiabetic agent in medical applications, the effect of antidiabetic activity of curcumin obtained after ethanolic extract of *Curcuma longa* rhizome can be enhanced via formation of silver nanoparticle by nanotechnology process, the results revealed that CSNPs showed effective antidiabetic activity against streptozotocin induced rats. Hence it can be concluded that nanosize particle of curcumin was more effective in inhibition of blood glucose level.

Table 1: Effect of curcumin extract loaded silver nanoparticles on fasting blood glucose level in streptozotocin induced diabetic rats

Treatment	Dose	Blood glucose level (mg/dL)					
		Normal	After induction of streptozotocin	1 st day	3 rd day	5 th day	7 th day
Control	Streptozotocin	84±2.5	231±1.19	249±0.5	263±0.85	278±1.1	287±1.17
Standard	Metformin	80±1.15	232±1.14	156±0.35	111±1.15	91±0.5	79±0.55
Test	CSNPs	81±0.78	234±1.11	168±1.15	115±2.12	94±1.35	82±0.5
	Plain curcumin	79±0.85	225±1.15	198±2.1	157±1.19	131±0.5	111±2.21

Data represented as Mean ± SEM (n=6)

Table 2: Effect of curcumin extract loaded silver nanoparticles on body weight in streptozotocin induced diabetic rats.

Treatment	Dose	Initial body weight	Body weight after 7 th day
Control	Streptozotocin	168±0.5	169±1.34
Standard	Metformin	169±2.21	168±1.15
Test	CSNPs	170±0.5	168±0.36
	Plain curcumin	170±1.19	169±0.5

Data represented as Mean ± SEM (n=6)

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Conflict of Interest: None declared

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