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Antidiabetic Potential of Copper Oxide Nanoparticles Using Biological and Polymer Functionalized Method Mediated by *Sarcostemma acidum* Stem Extract

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ABSTRACT

The nano sized copper oxide material (CuONPs) were prepared by the greener way and an approach functionalized by polymer using *Sarcostemma acidum* stem extracts. The *In vitro* anti-diabetic activity was studied through the α-glucosidase and α-amylase inhibitory methods were demonstrated in *Sarcostemma acidum* stem, biological synthesized CuONPs and polymerized CuONPs. The percentage inhibition at 100 µg/mL, 200 µg/mL, 300 µg/mL, 400 µg/mL and 500 µg/mL concentrations of *Sarcostemma acidum* stem, biological synthesized and polymerised CuONPs showed dose dependent inhibition in α-a m ylase and α-glucosidase. Throughout the studies, polymerized CuONPs showed highest inhibition of α-amylase and α-glucosidase as compared with green synthesis.

Keywords: *Sarcostemma acidum*, Copper oxide nanoparticles, α-amylase, α-glucosidase, Antidiabetic activity.

INTRODUCTION

W.H.O (World Health Organization) reported that approximately 80% of the world's population practiced the 'traditional medicines'. They are act as a primary health care in both developed and developing countries where the contemporary (modern medicine) medicines are largely used. The plant kingdom is the virtual goldmine of potential drug targets and it provides numerous pharmacologically active pharmacophores.[1,2] Around one-third of the top selling drugs in universe are natural products and their derivatives.

Mostly the natural products are widely recognized by the pharmaceutical industries for their structural diversity and its pharmacological activities. Totally 2,50,000-5,00,000 plant species are exiting on the planet and only 1-10% are used as foods by humans and animals. Now-a-days the plant materials get increasing interest on their applications in nutritional, pharmaceutical, nanoscience and cosmetic fields.[3,4] Nanotechnology is currently used as an instrument to research the darkest ways in medicine. As a result, nanoscale organic and inorganic particles are receiving increasing attention

in medical applications, due to their amenability to biological functionalization. Advances in nanotechnology have led to significant development in various areas, including nanoparticles, nanotubes and the synthesis of nanofils[5,6]. The medicinal plant extract mediated metal oxide nanoparticles were recently got attention which are more popular due to its eco-friendly approach, low-cost, and no or less toxic compared with the physical and chemical procedures. The concerns about of toxic effects of the CuO nanoparticles have particularly attracted toxicological researchers in recent years[7,8].

From the previous studies numerous plant mediated copper oxide nanoparticles has been studied which gain more attention owing properties like electrical, mechanical, magnetic and optical activities. Because of the properties it possess wide range of usages among the scientist and the researchers. Especially, it has the highest importance in all the physical, life and environmental sciences. Green synthesis is a profitable alternative that respects the environment and takes better account of physical and chemical methods, the biosynthesis process has many advantages in the synthesis of nanoparticles. Plants are a better platform for the production of nanoparticles because they are free of dangerous chemicals and contain natural closures. Biological synthesis is considered a kind of connection strategy, although it produces nanoparticles by reducing metallic particles by biomolecules in plants[9,10]. Diabetes mellitus is a metabolic syndrome associated with serious physiological imbalances. It is characterized by chronic hyperglycemia, which leads to several biochemical defects and oxidative stress. The main objectives of the present work is to investigate the antidiabetic activity of *Sarcostemma acidum* stem, biological and polymer functionalized copper oxide nanoparticles in comparative aspect. In this work two different copper oxide nanoparticles were synthesized and their *In vitro* anti-diabetic activity was screened which have not yet been investigated.

MATERIALS AND METHODS

The *Sarcostemma acidum* plant was collected in January 2020 in the village of Kathadipatti in the Thanjavur district in Tamil Nadu from a single herb. The plant was authenticated by Dr. S. John Britto, Director, Rapid Herbarium and Center for Molecular Systematics, S t. Jo se ph 's College. India. Acopy of Voucher specimen (V.P.001) was made in the herbarium.

Preparation of aqueous extract of Sarcostemma acidum

250 g of *Sarcostemma acidum* powder is taken in 500 mL beaker to that, 500 mL of double distilled water is added and boiled for 2 to 5 hours. After that, the beaker kept for cooling and followed by filtered by filter paper. Filtered extract is concentrated and stored in refrigerator for the further analysis.

Synthesis of CuO nanoparticles using stem extract

0.1M concentration of copper acetate monohydrate was prepared in 100 mL standard flask. From that, 20 mL of copper acetate solution was taken in a 100 mL beaker and kept on a magnetic stirrer and to that 80 mL of aqueous extract of *Sarcostemma acidum* stem was added dropwise. After the complete addition of extract, the whole mixture was stirred for 5 hours. Then left for an overnight. Final colloidal form of the solution was centrifuged at 6000 rpm. Collected nanomaterials were washed by water and followed by ethanol. Then heated at 150°C for the complete reduction of copper hydroxide to oxide form.[11,12].

Synthesis of polymer functionalized copper nanoparticles

For the synthesis of copper nanoparticles, which were functionalized by polymer in 100 mL of ultra-pure water, 0.2 g PVP (Polyvinylpyrrolidone) was dissolved and stirred at 80°C for 1 hour. After that, the solution was gradually added to the homogeneous CuONPs solution generated from the stock extract. After 1 h the light yellow of the mixture was converted into light brown color. The reaction mixture was able to cool down for 10 min and after being centrifuged at 10,000 rpm. The precipitates formed were washed with deionized water (D.D) and then dried in an oven at 70°C for 24 hours.[13,14]

Antidiabetic activity

In vitro anti-diabetic activity was carried out by the method of Apostolidis[8] using α-amylase and α-glucosidase enzymes.

RESULTS AND DISCUSSION

Our earlier report that the synthesized and

characterization biological copper oxide nanoparticle (30-70nm) and polymer functionalized copper oxide nanoparticle (27-32nm)[15].

***In vitro* anti-diabetic activity**

Diabetes mellitus is a known endocrine disorder and is more common in India today. The reason can be lifestyle and genetic factors[16]. One of the most serious and common causes of morbidity and mortality in the world is diabetes and the complications associated with it. Mixed diabetes (DM), a metabolic disorder, is characterized by chronic hyperglycemia, which is induced by a reduction in insulin synthesis or the insensitivity of body cells to insulin. Type 2 diabetes mellitus (T2DM), known as non-insulin dependent diabetes mellitus (NIDDM) is a chronic metabolic disorder characterized by postprandial hyperglycemia (PPHG)[17].

The digestive enzymes like α-amylase and α-glucosidase can hydrolyze starch, which are involved in the postprandial hyperglycemia. Inhibition of these two enzymes can reduces the release and absorption of glucose in the small intestine. Such inhibitory effects of nanomaterials on antidiabetic effect, can attributed to the evaluation of anti-diabetic activity[18.19]. The drugs Acarbose, voglibose and miglitol are the well-known examples of synthetic drugs which can block the enzymes. However, their use is limited or discouraged due to stomach pain, bloating, diarrhea, and other side effects. Consequently, from the green synthesis of nanoparticles, new inhibitors with improved safety and effectiveness profiles should be discovered and developed in order to effectively reduce postprandial glycemic levels. A decrease in PPH is most important because it helps to reduce the formation of advanced glycation end products AGE, a metabolite identified as a major risk factor for cardiovascular complications in DM patients[20]. In particular, it has been suggested that drug therapies for the activity of α-amylase and α-glucosidase may be beneficial to patients with DM with altered insulin nutritional reactions, especially other oral hypoglycemic drugs when used in combination[21]. The possibility of limiting weight gain and improving weight loss in non-diabetic patients has also been proposed[22].

The *In vitro* anti-diabetic activity was investigated through α-amylase and α-glucosidase inhibitory assay were proved in *Sarcostemma acidum* stem, biological synthesized CuONPs and polymerized CuONPs. The stem of *Sarcostemma acidum*, biological synthesized CuONPs and polymerised CuONPs showed maximum α-amylase inhibitory activity was 77.08%, 81.05% and 83.70% at concentration range from 100 to 500 µg/mL respectively (Table 1 and Fig. 1). The standard drug as Acarbose is used to compare the inhibitory activity. Acarbose at a concentration of (100-500 µg/mL) showed α-amylase inhibitory activity from 21.98 to 90.06% at the same concentrations 100 and 500 µg/mL respectively.

The *Sarcostemma acidum* stem, biological synthesized CuONPs and polymerised CuONPs showed maximum α-glucosidase inhibitory activity was 79.90%, 82.84% and 86.43% at concentration from 100 to 500 µg/mL respectively (Table 2 and Fig. 2). Different concentrations 100-500 µg/mL) of Acarbose showed maximum α-glucosidase inhibitory activity was 93.62%.

Table 1: *In vitro* anti-diabetic potential (α-amylase inhibition) of *Sarcostemma acidum* stem, biological synthesized CuONPs, polymerized CuONPs and compared with standard Acarbose at different concentrations

Concentrations (µg/mL)	*Sarcostemma acidum*	% of inhibition CuONPs (Biological Method)	Polymerised CuONPs	Std. (Acarbose)
100	17.61±0.19	18.54±0.23	19.07±0.26	21.98±0.31
200	25.96±0.23	29.66±0.33	35.18±0.41	40.92±0.48
300	47.94±0.39	51.39±0.51	54.03±0.55	58.79±0.61
400	59.86±0.56	62.79±0.63	67.09±0.84	75.49±0.89
500	77.08±0.79	81.05±0.81	83.70±0.96	90.06±1.02
IC_{50} Value (µg/ml)	328.28	308.21	288.69	256.42

Value was expressed in average triplet ± SD

Table 2: *In vitro* anti-diabetic activity (α-glucosidase inhibition) of *Sarcostemma acidum* stem, biological synthesized CuONPs, polymerized CuONPs and compared with standard Acarbose at different concentrations

Concentrations (µg/mL)	*Sarcostemma acidum*	% of inhibition CuONPs (Biological method)	Polymerised CuONPs	Std. (Acarbose)
100	18.46±0.17	19.77±0.20	21.89±0.23	24.67±0.25
200	31.56±0.22	35.78±0.36	38.23±0.42	43.13±0.45
300	48.52±0.41	53.10±0.48	57.69±0.55	63.88±0.63
400	69.60±0.63	72.50±0.65	76.14±0.79	80.71±0.86
500	79.90±0.78	82.84±0.89	86.43±0.96	93.62±1.04
IC_{50} Value (µg/ml)	302.47	282.75	263.59	236.13

Value was expressed in average triplet ± SD

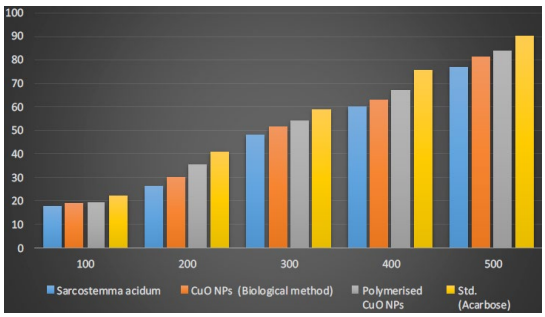

Fig. 1. *In vitro* anti-diabetic activity (α-amylase inhibition) of *Sarcostemma acidum* stem, biological synthesized CuONPs, polymerized CuONPs and compared with standard Acarbose at different concentrations

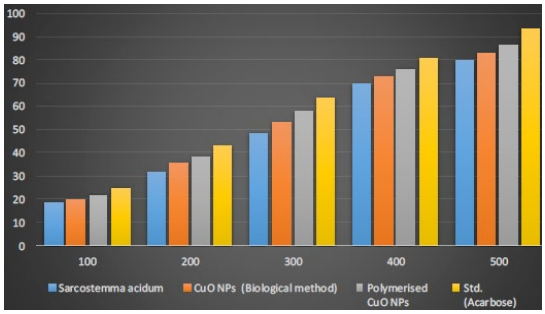

Fig. 2. *In vitro* anti-diabetic potential (α-glucosidase inhibition) of *Sarcostemma acidum* stem, biological synthesized CuONPs, polymerized CuONPs and compared with standard Acarbose at different concentrations

Inhibition rate of different concentrations (100 to 500 µg/mL)of *Sarcostemma acidum* stem, organic synthesis CuONPs and polymerization CuONPs show dose-dependent inhibition with α-amylase and αα-glucosidase. From this study, it can be concluded that CuO polymerization nanoparticles showed significant antidiabetic effects on α-amylase and α-glucosidase activity. I agree with Ghosh *et al.,* study[23]. Synthetic CuONPs has moderate levels of inhibition against α-amylase and α-glucosidase enzymes. This is comparable to the percentage of inhibitions caused by the Dioscorea bulbifera extract. Reduced availability of α-amylase enzymes and starch in enzymes on the surface of the fiber leads to reduced α-amylase activity[24,26].

CONCLUSION

Excellent inhibitory activity of CuONPs against α-amylase and α-glucosidase, which are considered to be important pharmacological targets for the treatment of T2DM. The high power output of these biological CuONPs for the inhibitory activity of glycosidase *In vitro* provides solid scientific evidence of CuONPs potential for anti-diabetes treatment and management of T2DM. The maximum *In vitro* antidiabetic activity of polymerized copper nanoparticles has been observed compared to biosynthetic copper nanoparticles and *Sarcostemma acidum* stem extract.

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Conflict of interest

There is no conflict of interest.

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