

Improvement of Glucose Tolerance and Related Metabolic Disorders Using Some Ayurvedic Mineral Preparations (Bhasmas) – in Nanomedicinal Perspective

Choudhary BK¹ and Kar A^{2*}

¹Department of Chemistry, A.S. College, Deoghar, Jharkhand, India

²Satsang Herbal Res. & Anal. Lab. Satsang, Deoghar, Jharkhand, India

*Corresponding author: Dr. Ajit Kar, Satsang Herbal Res. & Anal. Lab. Satsang, Deoghar, Jharkhand, India, Tel: 9709-278761; E-mail: karkbc2006@rediffmail.com

Received date: Oct 08, 2015; Accepted date: Nov 17, 2015; Published date: Nov 23, 2015

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Abstract

In the present study giving emphasis on diabetes mellitus, we have taken up some specialised Ayurvedic metallic preparations (Bhasmas) like Yasada (Zn), Vanga (Sn) and Naga (Pb) Bhasmas and also Swarna (Au), Raupya (Ag), Makardhwaja (HgS) Bhasmas used in related metabolic disorders (dyslipidemia, stress related and certain immune system disorders including ageing related complications). Though metals are not antidiabetic as such, the role of some mineral elements in the management of impaired glucose tolerance (early sign of diabetes mellitus) was well established. Also increased oxidative stress is found to be associated with the progression of diabetes mellitus and different metabolic disorders. Some metallo-enzymes like arginase, pyruvate carboxylase, manganese-superoxide dismutase are found to be beneficial in this regard. Further, it is known that nano-materials below 100 nm scale show reduced toxicity towards mammalian host and increases toxicity towards infectious organisms. As such, next for the measurement of the particle size (in nano scale) of the above Ayurvedic preparations, Transmission Electron Microscope (TEM) was used. Surprisingly all the above experimental samples are found to be within 100 nm scale and thus eliminating the risk of toxicity when used in prescribed dose. For example: Yasada Bhasma (12.5 nm), Vanga Bhasma (12.1 nm), Naga Bhasma (12.5 nm), Swarna Bhasma (12.2 nm), Raupya Bhasma (51 nm) and Makardhwaja Bhasma (39 nm).

Keywords: Ayurvedic mineral bhasmas; Diabetes and metabolic disorders; Albino rats; Nanomedicine

Introduction

Metabolic disorders like diabetes mellitus (type 2), dyslipidemia, especially ageing process start due to general decline in the physiological processes resulting in the disturbances of metabolic homeostasis. It is known that activities of many physiological/metallo enzymes and their co-enzymes play very significant role in this regard e. g. Zinc is present in many enzyme systems that are concerned with different metabolism [1,2]. Impairment of glucose tolerance is the early sign of diabetes. Diabetes mellitus is alarmingly increasing worldwide and inviting major health problems especially from its complications. It has been noted that a reduced secretory response to insulin with or without increase in peripheral resistance to its action, leads to glucose intolerance, which is an important factor causing diabetes mellitus. Further, the role of some mineral elements (Ca, K, Cr, Mn, & Zn) in the impairment of glucose tolerance and diabetes mellitus was well established [3,4]. We also reported the extra ordinary role of inorganic parts (containing different major & trace mineral elements) of different antidiabetic medicinal plants in the improvement of glucose tolerance [5,6].

In Ayurvedic system of medicine, the uses of different herbo-minerals and mineral Bhasmas (processed fine powder) have got its own place in the treatment of various diseases. Here to avoid toxicity from bulk consumption, purification of metallic Bhasmas is first carried out by heating thin sheets of metal repeatedly followed by macerating and plunging them into various herbal juices or decoctions

– till these are converted into fine powders. In the present study we have selected three standard Ayurvedic Pharmacopoeial preparations (Bhasmas) namely Yasada (Zn), Vanga (Sn) and Naga (Pb) extensively used in the management of diabetes mellitus and three others: Swarna (Au), Roupya (Ag) and Makardhwaja Bhasmas used in the management of ageing related metabolic disorders including diabetic dyslipidemia.

Next we took up characterization of these Ayurvedic Bhasmas and their role in nano-material perspective. Nanotechnology deals with manipulation of material particles at nanometer scale and has wide application in drug delivery system. Further, it is known that nano-material below 100nm scale show reduced toxicity towards mammalian host and increases toxicity towards infectious organisms. It is due to the presence of electronic effects brought about as a result of changes in the local electronic structures of the surfaces due to small sizes <100nm [7,8].

Methods and Materials

Oral glucose tolerance test (GTT) studies were performed on fasting Charles Foster strain white albino rats weighing between 150-200 gm body weights. The animals (C.F. Strain white albino rats) had liberal access to standard laboratory pellet diet and water ad libitum except during previous night of the experiment when no diet was given. Six animals were selected for experimental including control groups. The animals were fed orally 1.75 gm. glucose per kg body weight (dissolved in distilled water) along with the single dose of the experimental sample. The control group was given vehicle solution with glucose (1.75 g p.k.b.) only. Blood was collected at 0 hour, 1 hour, 2 hours and 3

hours intervals. Blood glucose was analyzed using the Trinder's Glucose oxidase method [9].

GTT studies were carried out using carefully prepared (as per approved Ayurvedic Texts) Ayurvedic metallic Bhasmas: Yasada (Zn), Vanga (Sn) and Naga (Pb) Bhasmas (kept in desiccator). To select the dose of the finely powdered samples, adequate precaution was taken to avoid metal toxicity. For this, recommended dietary allowances by the Food and Nutrition Board, USA was thoroughly consulted. The dose calculated and selected was 90 mg sample per kg body weight - suspended in 2% gelatin (Pharmacoepoeial grade) in warm water as vehicle solution. Next for the measurement of the particle sizes of the experimental samples in nano scale Transmission Electron Microscope (TEM) was used in the Department of Materials Engineering, I. I. Sc, and Bangalore.

Experimental Results

Blood glucose values reported as mean +SD (mg/dl) from six animals of each group. The effect of the single dose of experimental

sample on oral glucose tolerance test (GTT) recorded in the results of Table 1 below.

Time in hours after glucose load				
Sample	0 hr	1 hr	2 hrs	3 hrs
Control	78 ± 9	126 ± 6	76 ± 8	75 ± 7
Vanga Bhasma	72 ± 8	89 ± 2*	65 ± 5	61 ± 3
Naga Bhasma	84 ± 2	91 ± 9*	77 ± 8	71 ± 3
Yasada Bhasma	77 ± 2	94 ± 4*	73 ± 4	72 ± 4

Table1: Blood Glucose Values in mg dL-1. *Most significant compared to control (1 hr) blood glucose values (p<0.01). Also experimental results are represented graphically below.

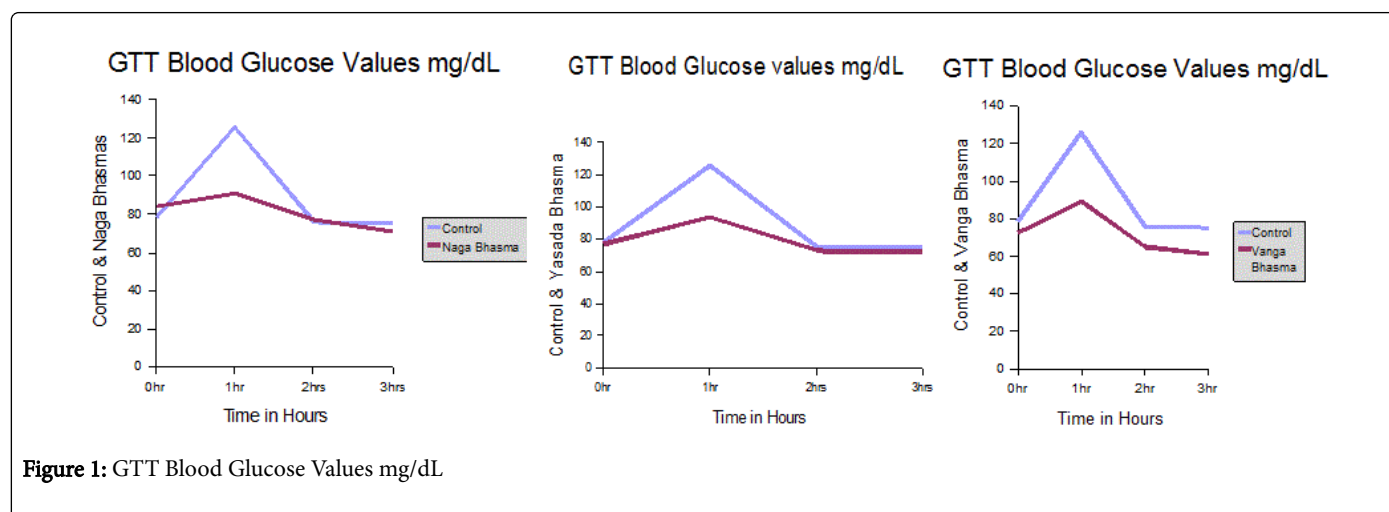


Figure 1: GTT Blood Glucose Values mg/dL

After that we have taken up the characterization of the following six samples (viz. Vanga (Sn), Naga (Pb), Yasada (Zn), Swarna (Au), Roupya (Ag) and Makardhwaja (HgS) Bhasmas) – in nano scale using Transmission Electron Microscope (TEM) and results shown below pictorially.

TEM Pictures of the Bhasmas under Study

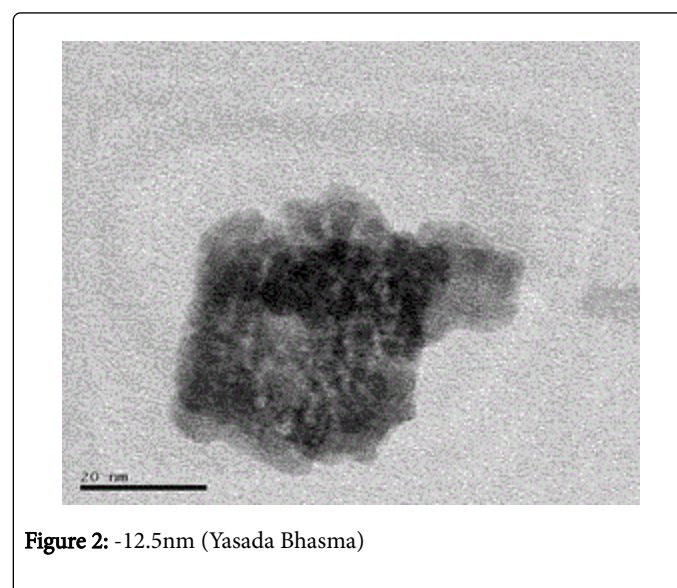


Figure 2: -12.5nm (Yasada Bhasma)

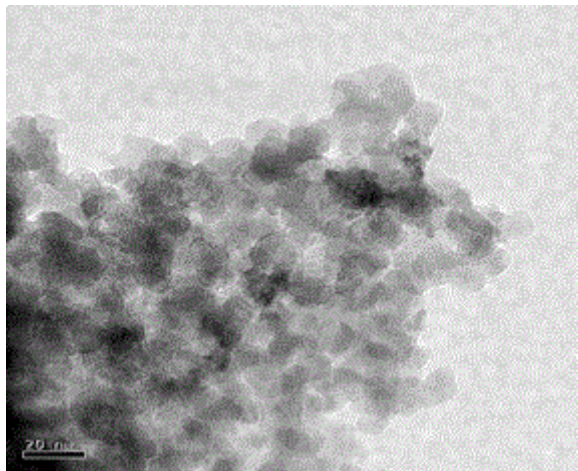


Figure 3: 12.1nm (Vanga Bhasma)

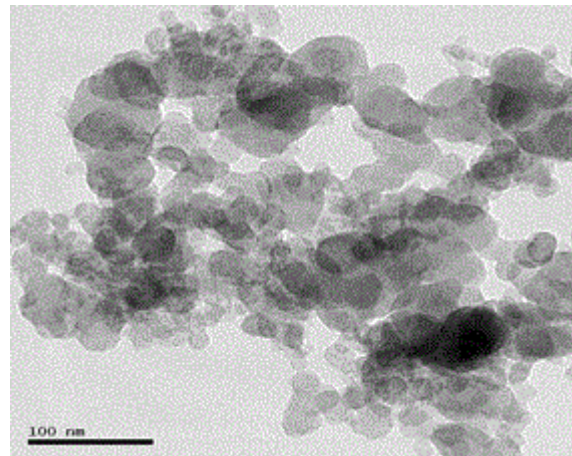


Figure 5: -51nm (Raupya Bhasma)

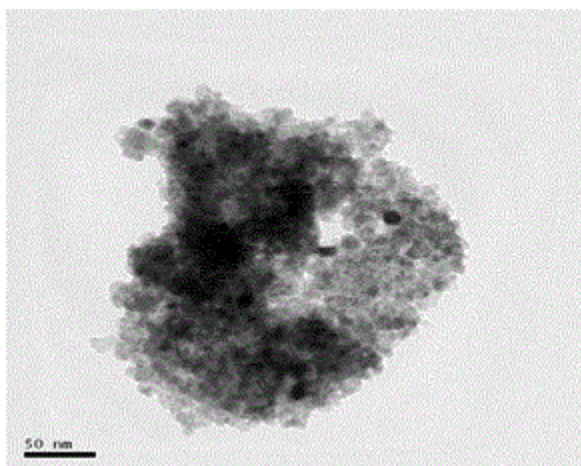


Figure 4: -12.5nm (Naga Bhasma)

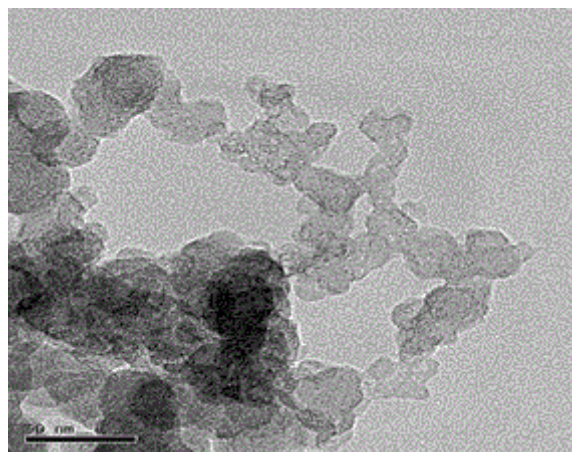


Figure 6: - 12.2nm (Swarna Bhasma)

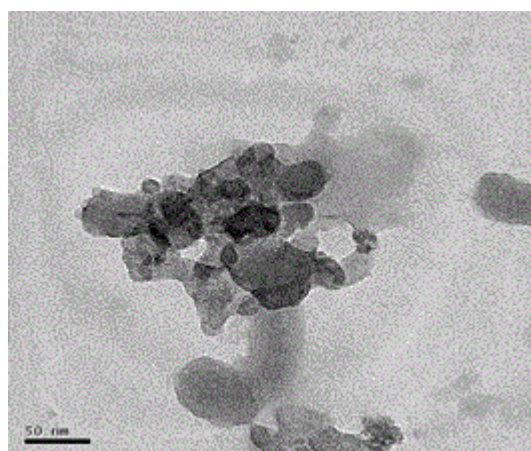


Figure 7: - 39nm (Makaradhwaja Bhasma)

Discussion and Conclusion

In normal glucose tolerance test peak blood glucose value is noted within ½ to 1 hr after glucose fed. The value gradually comes down close to 0 hr fasting level within 2 hrs. Close study of the above result in Table 1 indicates that experimental Ayurvedic Bhasmas are showing not only lower peak blood glucose values 1 hr after glucose load, the values are mostly not exceeding the usual highest normal fasting blood glucose values (100 - 110 mg/dl) and thus maintaining blood glucose homeostasis -which is very significant. These are also shown through the graphs plotted above. Further the role of some mineral Bhasmas e. g. Swarna (Au), Roupya (Ag) and Makardhwaja (HgS) in the management of age related metabolic disorders (diabetic dyslipidemia, arthritis, certain immune system disorders etc) are well known.

While studying from nano-medicinal perspective surprisingly all the particle sizes of the above experimental samples (reported in TEM picture) have been found to be much below 100 nm scale and thus eliminating any risk of toxicity in the host body. This is especially significant in the case of Makardhwaja (HgS). Because mercury as such is very toxic and Makardhwaja (in prescribed dose) has been in use for more than thousand years without known side effects. In fact the ancient Ayurvedic practitioners were preparing above mentioned mineral Bhasmas in nano meter particle sizes (knowingly or unknowingly) – confirmed through our studies. Besides, it has been reported that some Ayurvedic Bhasmas (Tamra Bhasmas etc) when given in high doses to experimental rats does not get absorbed in the gastrointestinal (GI) tract, but gets excreted [10].

It is also to be noted that though the experimental Ayurvedic samples are not as such hypoglycaemic agents, these are very efficient in maintaining blood glucose homeostasis besides improving impaired glucose tolerance. Probably the specific inorganic mineral elements present in the experimental samples either promoting or inhibiting the activities of specific enzymes along with the improvement in insulin response, release or activity. Metabolic disorder generally starts due to gradual decline in the physiological processes resulting in the disturbance of the different intracellular metabolic homeostasis. Further, overall consumption of conventional drugs have got some side effects which can be lowered significantly by the delivery of active drug molecules in considerably lower dose than needed, through nano-medicinal technology. Some recent potentially important application includes cancer treatment with gold and iron nanoparticles [11].

Lastly, indiscriminate use of metallic Bhasmas is not encouraged to avoid toxicity. We have studied only the above mentioned Ayurvedic Bhasmas in nano-medicinal perspective.

Acknowledgment

We are grateful and thankful to Dr. G.S. Awadhani and Dr. Govinda Swami for the measurement of particle size of the experimental samples in nano-scale using Transmission Electron Microscope (TEM) with kind permission from Prof. V. Jayaram, the then Chairman, Deptt. of Material Engineering, I. I. Sc. Bangalore. Also, we are thankful to Porofessor C. B. Jha, HOD,Rasashastra and Dean Faculty of Ayurveda, IMS, BHU – for his valuable suggestions as and when needed.

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