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CONCEPT OF NANO TECHNOLOGY IN SIDDHA MEDICAL LITERATURES

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ABSTRACT

The unique feature of Siddha Medical System is its vast and complex pharmacology. The raw materials used in *Siddha* medicines are of plant, metal, mineral and animal origin. The extensive use of herbo-mineral formulations is considered as high order. The preparation of majority of medicines involves tedious processes which result in physico-chemical transformation of the particles size, chemical composition which regulates the bio-mechanism of the drug in the body, thus enhance the efficacy and reduce toxicity. Unique preparations of Siddha system of medicine like *Parpam*, *Chenduram*, *Chunnam*, *Kattu* and *Padhangam* are 'life saving' and 'miracle' nanomedicines, which were prepared by the *Siddhars* on the basis of nanotechnology. Recent advances in science explored the nano particles, which find potential usage in bio-medical field especially in cancer, degenerative diseases. Though the concept and utilization of nanoparticle emerged in late twentieth century, Siddha medical system has theoretical references and practical application of nanoparticles from many centuries. This article reviews the presence of nanoparticle in Siddha medicines like *Linga Chenduram*, *Poorna Chandrodayam*, *Velli Parpam*, *Kshaya Kulandhaga Chenduram*, *Muppoora Chenduram*, *Thanga Parpam*, *Naga Parpam*, *Naga Chenduram*, *Chara Parpam* etc., with the aid of modern technology like SEM with EDAX, FTIR, ICP-OES, XRD, DLS etc., their usage as per literature and how these nano particles are being used in different fields.

KEY WORDS: Siddha Medicines, Nanoparticles, Parpam, Chenduram, SEM, DLS.

INTRODUCTION

The unique feature of Siddha medical system is its vast and complex pharmacology. The raw materials used in Siddha medicines are of plant, metal, mineral and animal origin. The rich flora of our country is selectively utilized for the welfare of mankind. Apart from this, the ancient synthetic chemico-philosophical system developed by *Siddhas* has huge treasures in the name of medicines and teaches healthy way of living. The extensive use of herbo-mineral formulations is considered as high order. Siddha medical system uses chemico-metallurgical medicines of 212 varieties namely metals, minerals, salts, arsenics, mercury and sulphur as medicines.[1] The raw materials are purified and processed as described in literature and used for therapeutic purposes. The eminent medical-chemists of the olden days excelled in alchemy, which aims at transformation of baser metal to higher metal by minerals, plant sources and by animal products. The innate quality of the drug is transformed from one form to another to make the particles assimilable in the human system by the digestive processes.

The herbo-mineral drugs are generally soaked and triturated with herbal juice or decoction. The herbs which are used in these processes are very specific, according to the metal or mineral used. Then the drug is subjected to incineration or sublimation and again triturated. The drugs undergo tedious processes during preparation and result in physico-chemical transformation leading to reduction in particle size and its chemical composition which regulate the bio-mechanism of the drug in the body, thus enhance the efficacy and reduce toxicity.

Unique preparations of Siddha Medical System like *Parpam, Chenduram, Chunnam, Kattu* and *Padhangam* are called 'life saving' and 'miracle' medicines. Most of the medicines of the above category were found to contain nanoparticles and it seems *Siddhas* had used special techniques to prepare each and every medicines. Recent advances in science explored the nanoparticles, which find potential usage in bio-medical, optical, electronic, automobile and space research. Though the concept and utilization of nano particle emerged in late twentieth century, Siddha medical system has theoretical references and practical application of nanoparticles since time immortal. This article reviews the exploration of nanoparticle in Siddha medicines with the aid of modern technology like SEM with EDAX, FTIR, ICP-OES, XRD etc., and their usage as per literature.

In general, Particles are classified into three. They are Coarse particles (10,000 – 2,500 nm), Fine particles (2500 – 100 nm) and Ultra fine particles or nano particles (1- 100 nm).

Nanomedicine is the application of knowledge of nanotechnology in science and medical procedures. It is a field of applied science devoted to the control and manipulation of matter on a scale smaller than one micrometre, i.e., at the level of atoms and molecules (nanomaterials). The most common is that such manipulation occurs in a range of between one and one hundred nanometers.

HISTORY

Many Siddha nano-medicines are already in routine clinical practice and are claimed to be the very effective and potent. According to the current Nanoscience, the commonest definition of nanotechnology is said in relation to the width of a human hair (M.A.Shah and Tokeer Ahmad). Human hair is about 60-80,000 nanometers wide.[2] But this concept of nanoscience goes back to ancient times, and is as old as the *Thirumandhiram* and *Thirukural.*

In *Thriumandhiram,* the *Siddha Thirumoolar* mentioned about atomic theory in 7th Tanthram-verse, 2011 which is related to the nanoscience. In many places he used the word *'Anu'* which refers to atom.

In the above lines, *Thirumoolar* describes the size of the soul. He pioneered in his attempt and said that the size of a soul is approximately equivalent to one in lakh of a hair shred of tail of a cow. Note that the said hair should be split along the grain i.e. it should be split vertically and not horizontally. This is tantamount to say that the size of the soul is far smaller that it is as invisible as an atom.

One of the eminent Tamil Poets, *Avvaiyar* compared the contents of the treatise *Thirukkural* with the immeasurable things in an atom (nano-science), when it is pierced. In the following verses, she says that an atom can be pierced and it contains enormous and deeper things which can store seven seas of the world.

The concept of atomic theory is not new to Tamil Tradition. The importance of group of atoms *(anuthiral)* in the production of speech is said in the following lines of *Nannool* [3] as

SYNTHESIS

In modern nano technology various techniques are advocated to synthesize nano particle like attrition, pyrolysis, inert gas condensation, radiation chemistry, hydrolysis, poly condensation, precursor sol etc. In Siddha Medical system, these nanomedicines were prepared by triturating the raw drug with herbal juice, then subjected to incineration in an

earthen pot for certain hours, then cooled and again triturated. The nanomedicine thus produced is economical and highly therapeutic when executed with intense knowledge.

PROPERTIES AND BENEFITS

Nanoparticles exhibit unique physico-chemical properties such as ultra small size, greater surface area per weight than larger particle and high reactivity. They can deliver drugs at cellular and nuclear level. They are proved to be more effective since they improve the drug bio-availability. It can be administered via different routes. Stability of nano-particles offers the possibility of oral administration. Nanoparticle mediated delivery may provide a means of alternate route, circumvenating the blood brain barrier.[4]

The utilization of nanotechnology for the benefit of human health and well being is called nanomedicine. The application of nanotechnology in various fields of medicine is used for diagnostics, therapeutics and as biomedical tools for research.[5] This provides treatment at a molecular level especially for cancer chemotherapy and anti-diabetic agents. Nanotechnology is applied in tissue regeneration, cell culture, targeted drug therapy, diagnostics, biosensors and molecular biology. They ensure greater degree of cell specificity, improves efficacy and minimize adverse effects.[4]

CHARACTERIZATION

Nano particles are analyzed through following techniques. Transmission Electron Microscopy (TEM), Scanning Electron Microscopy (SEM), Atomic Force Microscopy (AFM), Dynamic Light Scattering (DLS), X-Ray Photoelectron Spectroscopy (XPS), Powder X-Ray Diffraction (XRD), Fourier Transform Infra Red Spectroscopy (FTIR), Matrix-Assisted Laser Desorption/Ionisation Time-Of-Flight Mass Spectrometry (MALDI-TOF), UV Visibe Spectroscopy, Dual Polarization Interferometry, Nuclear Magnetic Resonance (NMR), Nano particle Tracking Analysis (NTA). NTA is done for tracking of Brownian motion. It helps to know the sizing of individual nano particle in solution.

DETERMINATION OF NANO PARTICLES IN SIDDHA MEDICINE

Siddha medicine are usually the mixtures of many constituents and the active principle in most cases is unknown. Hence scientific techniques like XRD, SEM with EDAX, FTIR, ICP-OES and TEM shall be employed to determine the physico-chemical finger print of the drugs. Presence of nano particles shall be tested by DLS. TEM shall be used to confirm the presence of nano particles. This article reviews the presence of nano particle in Siddha medicines like

Linga Chenduram (LIC), Poorna Chandrodayam (PC), Velli Parpam (VP), Kshaya Kulandhaga Chenduram (KKC), Muppoora Chenduram (MC), Thanga Parpam (TP), Naga Parpam (NP), Naga Chenduram (NC), Chara Parpam (CP) and its applications.

LIC is the prepared medicine made from cinnabar (Sulphides of Mercury), PC is a compound drug made of Mercury, Sulphur and Gold, VP is made from Silver, KKC has Arsenics, corals, sulphur etc., MC is made from Calomel, Cinnabar and Sulphide of Mercury, TP is made from Gold, NP and NC are made from Zinc, CP is made from Ammonium chloride and Potassium nitrate.[6, 7] SEM and EDAX provide good estimate of concentration of main elements in the samples. Analysis of LIC, PC, KKC, VP, CP was found to have difference in size and agglomeration of particles. Agglomeration is due to repeated cycles of calcinations involved in preparation.

SCREENING FOR NANO PARTICLES

Dynamic Light Scattering (DLS) shows the presence of nano particles. Out of three samples of LIC studied, it shown 10% of particles below 69.2 nm. PC showed particles close to nano, of which 10% of the particles are of 139.9 nm and 95% of the particles are of 613.6 nm.

Analysis of herbo-mineral formulation of Siddha medicine through TEM pictures, shows that particles are not of uniform size. There were more number of particles in range 40-50 nm in LIC and PC was slightly larger.[8] High Resolution Scanning Electron Microscopy of *Muppoora Chenduram* reveals the nano particle of size 83.3 nm.[9] which has smooth surface, spherical shaped and cumulatively distributed. *Chara parpam* has nano particles ranging from 14 nm, 19.5 nm, 20.5 nm, 30.2 nm to 268 nm.[10]

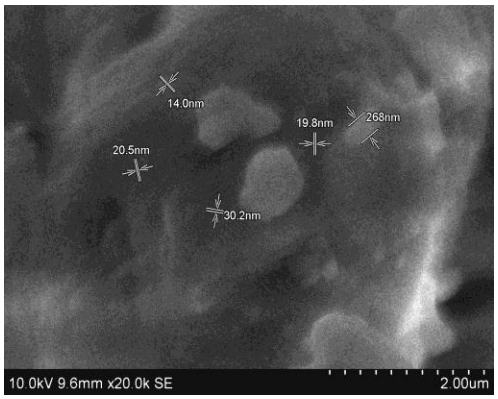

Fig No.1**: Showing nano particles in *Chara parpam*, analysed through SEM.**

NANO MERCURY

Mercury finds enormous usage in Siddha medicine in the treatment of cancer, auto immune diseases like Psoariasis, rheumatoid arthritis, Systemic lupus erythematosus, chronic ulcers etc. Mercury in different forms like calomel, cinnabar, red sulphide of mercury is widely used.

Three samples of LIC were studied in IIT, Chennai. Out of the three samples studied, one sample had increased number of nano particles which may be attributed to the method of preparation. ICP-OES confirmed mercury as the main component of LIC along with Ca, Cd, Cr, Cu, Fe, Mg at less than 1%. XRD showed standard peaks for HgS. EDAX and TEM confirmed the presence of HgS in the nano particle of LIC.[8] Sulphide of mercury is less toxic, less absorbed than any other forms of mercury such as elemental mercury or organic mercury. Acute toxicity study shows that low dose of HgS did not produce any toxic effects up to 7 days.[11]

NANO GOLD

The auspicious metal gold, in oxide form or sulphide form as *Thanga parpam or chenduram* is being used in Siddha medicine for the treatment of auto immune diseases, respiratory diseases, skin diseases, reproductive disorders and other chronic diseases.

The drug PC was found to have 10% particles of size near to nano particles. ICP-OES revealed that the main component of PC is mercury and it contain gold of 0.8mg/g. *Thanga parpam* has globular particles of gold with size 56-57 nm [12].

Nano gold is proved to be effective in ameliorating the symptoms of mycobacterial collagen-pristane induced arthritis in rats. Chronic administration of *Thanga parpam* (which contained Ag, Pb, As) showed no symptoms of liver and kidney toxicity in experimental animal model. Another study authenticated the use of gold as an antioxidant agent. Interestingly, chronic administration of TP treated animals showed significantly increased level of superoxide dismutase and catalase activity [13]. It is known that these two enzymes reduce the free radical concentration. Thus the antioxidant properties may have some role in rejuvenation of health. PC is one such a classical Siddha drug, advocated as a rejuvenative medicine (*Kaya karpam*)

NANO SILVER

Silver *(velli)* is used in Siddha Medical System for respiratory diseases, haemorrhoids, venereal diseases etc.[14] SEM and EDAX shows that VP has increased Ag, Ca, O_2 as silver oxides and calcium oxide. Particle size analysis by DLS showed the presence of particles of size 188.7 nm (10%) to 747.7 nm (95%).[8]

Silver nanomaterials are used in treating external infections for better wound healing and antimicrobial properties.[15] Silver has strong anti microbial properties in both metallic and nano form[16]. Silver nano particles were found to have inhibitory activity against human immunodeficiency virus (HIV), hepatitis B virus (HBV) and H1NI Influenza A virus[17].

NANO ZINC

Zinc is very essential to carry out physiological processes of the body. This micro mineral helps balance carbohydrate metabolism and blood sugar, increase metabolic rate, required for gene transcription, boosts immune system, regulate smell and taste sensation.

XRD confirmed the presence of standard ZnO in NP and NC. ICP-OES shows NP has zinc and calcium of 388, 39.7 mg/g respectively. NC also had relatively same amount of zinc and calcium. DLS showed the presence of nano particle of size 233.9 to 1374.2 nm in NP and 357.8 to 1711 nm in NC[8].

Zinc oxide nano particles were proved to be effective against both gram positive and gram negative bacteria. It has antibacterial activity against even high temperature resistant and high pressure resistant spores. The interaction between the bacterial cell and ZnO particles is due to electrostatic force [18]

TOXICITY

Though scientific studies reveal nanoparticle may produce toxic effects, it is not encountered with the administration Siddha nanomedicines. Because, recent studies explain that the wholesome of the particles in nano size induce cytotoxicity, but interestingly Siddha medicines constitute only minimum percentage of particles in a formulation are of nano size. Moreover, the sizes of the nanoparticles present in the Siddha formulation are of varying size and shape. This renders greater therapeutic value and less or no side effects.

In vitro and animal studies have shown that ingested nanoparticle can reach circulation and reach different organs and systems and possibly result in toxicity[19], but Siddha

nanomedicines which are administered orally from many centuries did not produce ill effects. This may be attributed to the method of preparation and dosage of the medicine. Even though, the Siddha nanomedicines are being used since centuries, its mechanism in the human body must be validated scientifically.

CONCLUSION

Presently, nanotechnology is very expensive and it is difficult to manufacture. But *Siddhas* practiced these types of medicine from time immortal at low cost and programmed methods. Although the concept of nanomedicine is recent to modern science, the traditional Siddha medicine has plenty of drugs of nano size with varied chemical characteristics. Extensive scientific research should be carried out to exhibit the therapeutic and toxicity effect of Siddha nanomedicines. This will help as a tool for standardization and quality control of herbo-mineral medicines, to reach the global community and for the welfare of mankind. The ancient tradition with treasures of medicinal chemistry is to be explored to the core, to unravel the mechanisms of these drugs with a scientific approach.

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