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**Review for Application of Nanotechnology in Ayurveda**

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*Abstract: The science and technology handling the particles for innovative medicines has attracted the world in last few decades. Indian government's idea to apply the technology is appreciating approach. Ayurveda discloses the already existing practices of nanotechnology with options of improvement. Increased surface area, enhanced bioavailability, rapid onset of therapeutic actions with reduced doses are expected with this technology. A detailed structure-based study of compounds from existing formulations as well as inventions of new formulations with basic formulations are having greater options of researches in this field. Minute understanding of nanotechnology have options for better application of medicines. DNA or gene-based responses of these compounds from formulations will guide for more efficacious personalized Ayurvedic medicines. Problems of safety and standard of Ayurvedic formulations can be solved using this technology in field of Ayurveda. Nanotechnology can be utilized both in diagnosis and treatment.*

**Keywords:** Nanotechnology, Ayurveda, Nanoparticle, Bhasma, Basti, Personalized medicine.....

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Nature gives clues for many phenomena, processes and concepts. The real apprehension of human mind takes time. Since the development of earth, nanoparticles are around human beings in forms of ashes, smokes, soot etc<sup>1</sup>. Hemoglobin that binds to protein is only 5.5 nanometers in diameter while a strand of DNA is only measured as 2 nanometers<sup>6</sup>. But, the clues took long time, until the concept was first discussed by *Richard Feynman* in 1959<sup>7</sup>. The term, 'nanotechnology' was first time coined by *N. Taniguchi* in 1974<sup>7</sup>.

The official website of 'United States National Nanotechnology Initiative' defines nanotechnology as, 'science, engineering, and technology conducted at the nanoscale, which is about 1 to 100 nanometers'<sup>2</sup>. It imparts new properties to materials<sup>3</sup>. Nanoparticles are those in range of 1-100 nm. The concept of nanotechnology lies with ability to control atoms and molecules for specific purposes in terms of novel materials and devices<sup>2</sup>. Processing for nanomaterial preparations changes the physical, chemical and biological properties from their larger counterparts<sup>4,6</sup>. Nanotechnology has penetrated deep in health sciences since 2010 with nano-enabled pharmaceuticals and medical devices<sup>5</sup>. Processes involved is targeted to ensure purity, efficacy and safety specifically for medical purposes. The nanotechnology is extensively utilized in recent past as delivery vehicles of therapeutic agents and imaging techniques<sup>9</sup>. Engineered nanoparticles are designed to pass through the barriers of body. The gap between interactions of molecules and cellular responses is filled by nanotechnology<sup>11</sup>.

The importance of nanoparticles was realized much before in *Ayurveda*, when the qualities of *Bhasma* was suggested to be adjudged based on fineness of its particles. Even the preparation of *Bhasma* includes the processes involving the mechanical and thermal energy with addition of various herbals to metal elements in number of cases. Studies on particle size of some *Bhasmas* reveal the particles' size in nanometers. FTIR (fourier-transform infrared spectroscopy) analysis of some *Bhasmas* have disclosed the attachment of functional groups with metals.

The *Government of India* launched the mission for promotional activities in nanotechnology in *May 2007* under *Department of Science & Technology*<sup>10</sup>. Ayurveda is one of competitive area where the options of application is demanding. Applications of nanoparticles is related with enhanced dose-response, improved bioavailability, increased solubility etc.

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### Concept Similarities with Ayurvedic Formulations

**Particle size related:** Nanoparticles are substances of 1-100 nm in size. Dhanya et. al. (2017) reported the particle sizes of *Yashada Bhasma* varying from 311 nm to 935 nm<sup>12</sup>. Similarly, many others have studied the particle size of different *Bhasmas* in range of 1-1,000 nm. Resin from oleo-gum-resin or gum-resin of herbal drugs used in Ayurveda also reveals the size of particles in range of 1-1,000 nm. However, agglomeration of particles due to distinguished physico-chemical properties and chemical reactivity of particles is common problem in both cases of *Bhasmas* and resins.

**Chemical reaction and bonding related:** *Bhavana* given during preparation of metallic drugs with addition of herbals' sap is supported by mechanical energy (*Mardana*) which increases kinetic energy of ions involved. Geometry and electronic properties of metals and organic networks are governed by the specific bonds on surfaces<sup>13</sup>. The reactivity of these organometallic compounds depends upon the ionic characters of carbon metal bonds<sup>14</sup>. Advances in ligand designing and catalysis have contributed to modern pharmaceuticals with new products<sup>15</sup>. A sufficient amount of energy causes breaking of bonds and formation of new bonds<sup>16</sup>. Reduction of metals occurs during preparation of formulation. Functional groups present in sap of herbals get attached to metals by various chemical processes including substitutional, electrophilic addition etc.

**Changes at molecular level:** These reactions during the course of preparation bring the changes at atomic and molecular level as revealed in FTIR analysis of *Bhasmas*. Chaudhary et. al. (2015) presented the stretching vibrations of C-Cl, C-Br, O-H, N-H, C=O etc. in *Tamra Bhasma*<sup>18</sup>. Sharma and Garg (2018) exhibited C-H, O-H, N-H, C-O and C=HO linkages in *Kukkutandtwak Bhasma*. Number of studies have shown similar changes at molecular level in preparation of different *Bhasmas*. Such changes bring the pharmacological effects by increasing interaction with target enzymes and enhancing the selectivity for receptors<sup>17</sup>.

### Advantages of Nanotechnology

**Increased surface area:** The surface area to volume ratio is dependent upon radius of particles. Smaller radius means increased ratio<sup>19</sup>. Smaller particles from slices of bigger particles get more surface area to exposed to conditions or surrounding environment. More number of atoms are available for interactions.

**Enhanced solubility:** Solubility is dissolution of given amount of substance at specified temperature in particular solvent. Increased surface enhances the dissolution rate of materials by bringing more particles in contact of solvent used for solution<sup>20</sup>. This results in overall increased surface energy of particles. Solubility is also directly related to molar surface area of particles. It also works to increase saturation concentration of liquid.

**Increased permeability and retention time:** Shape, size, density and surface functions of nanoparticles affect the permeability. The hydrodynamic areas outside and inside the particles required to be handled simultaneously, which disagrees much from those of solid impenetrable particles<sup>21</sup>. A modification in surface area makes the particles suitable for permeability. Such modifications are expected in *Ayurvedic* formulations. This also increases the retention time of drugs. A detailed screening is required for confirmation.

**Particle size distribution and bioavailability:** Khadka et. al. (2014) has illustrated the reduction in particle size to particle size to improve bioavailability of drugs<sup>22</sup>. Andrysek (2001) revealed relationship of the improvement of bio-

availability with particle size distribution<sup>23</sup>. More studies of *Ayurvedic* formulations in terms of particle size and combinatorial chemistry of particles of different ingredients and vehicles are required.

**Less dose requirement:** Required therapeutic dose of drugs in plasma or bioavailability of drugs is directly related with dose<sup>24</sup>. Nanoparticles are associated with increased dissolution, so more bioavailability. Smaller particles have more bioavailability with their larger counterparts. So, less dose is required.

**Rapid onset of therapeutic effect:** Dose and bioavailability are positively linked to response in drug-response curve. Faster absorption and bioavailability brings rapid onset of effects.

**Decreased variability:** Specialized engineering of nanoparticles change the surface kinetics. This makes them to opt with specific structure with less variability<sup>25</sup>. Standard operating procedures of formulations with needed improvement and measurement of particle size at stages give chances of reduction in variability.

### **Need of Nanotechnology in Ayurveda**

Marketing of groups of medicines from nanoparticles viz., conjugated drugs, liposomes etc. have increased to billions in a decade. Various organizations throughout the globe have forecasted for further jumps in market of nanoparticles' related products. In these circumstances Ayurveda is looking to understand its role in increasing the country's segment in trade of nanoparticles' related products as quality of products can be further improved for more acceptance across the world. Some of common problems existing with *Ayurvedic* products can be handled through nanotechnology.

**Ability to overcome solubility and stability issues:** Kashaya (decoction), Kalka (paste), Swarasa (sap), Hima (cold infusion), Phanta (hot infusion) etc. are important formulations of Ayurveda used as medicine directly or as part of many other formulations like *Asava*, *Arishta* etc. Solubility of components in decoction or sap or paste is common issues which can be settled with size reduction and changing the surface structure with medically inert compounds to avoid the aggregation of component particles and precipitation. Further reducing or stopping the naturally occurring enzymatic reactions in these formulations gives the chances to increase the shelf-life. Research is required with modified formulations and technologies giving the similar therapeutic effects without reduction in bioavailability. *Asava* and *Arishta* themselves produce self-generated alcohol through the process of fermentation which increases the shelf-life as alcohols are also antimicrobial<sup>26</sup>.

Rasa-shastra, a branch of *Ayurveda* deals with mineral or herbomineral products. Particle size reduction and consistency in size of particles is a big affair. Manufacturing with traditional methods and hesitation of utilizing the modern technologies at appropriate place are main reason behind this. An understanding with pharmacological mechanism is required with complete chemistry of raw materials and finished products for apprehension of introduction of technologies without affecting the therapeutic effects. Nanotechnologies have greater options in these cases to solve the problems specifically solubility of these products.

Oil and Ghrita are another formulations of *Ayurveda* where ingredients are brought to oil and Ghrita (ghee) vehicle through decoction and thermal energy application. Fatty acid profile is important for prediction of shelf-life of Oil and Ghrita. If primary and secondary oxidation is resisted to occur, the shelf-life of products are increased<sup>27</sup>. Int-

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reduction of nanotechnology to maintain the geometry and configuration of these fatty acids gives option to increase the shelf-life.

Many other formulations like *Guggulu* preparations, *Parpati* preparations etc. have further options to enhance the solubility and maintain the stability.

**Localize drug delivery:** By adjusting the electrospun matrices of compounds changes in physical, chemical and biological properties are imparted<sup>29</sup>. These fabrications of particles convey to desired drug delivery. Hou et. al. (2017) revealed the localized cancer treatment by introducing diffusion molecular retention (DMR) using transferrin modified CuS nanoparticles<sup>28</sup>. In *Ayurveda*, *Basti* procedures are applied as localized drug delivery depending on its types (*Niruha*, *Anuvasana* or *Brihmana*) and components used in *Basti*. Many of components are absorbed faster from intestine and act through path of systemic circulation. Various ointments and creams are used in *Ayurveda* where thickness of application is considered as important for topical application from absorption points of view. If nanotechnology-related rectification is exercised in these formulations, options of more and faster absorption cannot be negated.

The holistic approach of *Ayurvedic* medicines to act on every related system for curing or prevention from physiological alterations can be further improved by employing the nanotechnology.

**Individualized medicine:** *Charak Samhita Vimanasthana* 8/94 mentions the examination and treatment of patients based on individual's *Prakriti* (physical constitution), *Vikriti* (morbidity), *Sara* (tissue elements), *Samhanana* (compactness of organs), *Pramana* (measurement), *Satmya* (homologation), *Sattva* (psychic condition), *Aharashakti* (power of digestion of food), *Vyayamashakti* (power of exercise) and *Vayas* (age). These parameters are based on methods available at that time<sup>30</sup>. Even the concept of personalized medicine to diagnose and treat each patient similarly<sup>31</sup>. The basic difference comes with innovations of genetics concepts and their impacts on health. Actually the concepts of personalized medicine are separate from traditional practices of standard drugs for standard diseases. It is more concentrated on individual patient. Personalization of treatment with specific dose in distinguished cases based on genetic make-up is well supported by nanotechnology. This technology is used to determine DNA-sequencing using nanopores<sup>32</sup>.

### Scopes of Nanotechnology in Ayurveda

Revival and modernization is law of nature to survive. *Ayurveda* has never restricted itself from new inclusions. History suggests that many of drugs and techniques are added timely. Even detailed screening reveals the working of *Ayurveda* at molecular levels. Nanotechnology can be utilized to unfurl such details. Options are there for elaborated study of drugs. Compounds present with formulations and their structure are needed to be unveiled. Relationship of one compound on several systems and several compounds on one or several systems are needed to divulge the inside information.

Size-reduction and maintenance of same size in all cases are big challenge for *Ayurvedic* medicines. Possible uses of nanotechnology may bring this as true. Many new formulations on the basis of *Ayurvedic* concepts have options to be exhibited for novel and standard drug delivery. Applications of nanosensors, nanorobots etc. may contribute to idea. DNA-directed drug is a hope for *Ayurvedic* medicines with more additional researches.

**Conflict of Interest:** No Conflict of Interest

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