

Herbo Mineral Formulations (*Rasaoushadhies*) of Ayurveda An Amazing Inheritance of Ayurvedic Pharmaceuticals

Anand Chaudhary*, Neetu Singh,

Dept of Rasa Shastra (Ayurvedic Pharmaceuticals), Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

ABSTRACT

The one of the oldest system of medicine, Ayurveda is momentous in audience of worldwide on virtue of its holistic approach of life. Formulations of Ayurveda consist of substances of herbal, mineral/metal and animal origin which are processed pharmaceutically to have therapeutic effects. This is attribute of processes of *Shodhan* (purification/potentiation), *Bhavana* (impregnation/levigation) and *Marana* (incineration/calcinations) of *Rasa Shastra* which acclimatize these toxic industrial matter to a effective remedies known as herbo mineral formulations (*Rasaoushadhies*) of Ayurveda. In recent past there is prevalence of some doubt on safety and efficacy of these medicines. In this review paper we tried to justify application of these medicines as these are time tested and showed wonderful clinical adaptability. We also attempted to establish new facts of figures of core science in explanation of these medicines.

Key words: *Shodhan*'a-*Marana* *Bhasma*, Nanotechnology, Metallopharmaceuticals.

Introduction:

Ayurveda is the science of life which deals with maintenance of health of healthy persons and cure of ailing humanity as its main ambition^[01]. Ayurvedic doctrine of treatment is based on *Hetu*, (etiological factor) *linga* (symptom/manifestation) and *Aushadh* (medicine) and all these stand on concept of *Tridosha* (three fundamental humours), *Panchamahabhuta* (five basic of existence of cosmos), *saptadhatu* (seven vital functionaries of human physiology)^[02]. Ayurvedic physicians put into practice these all factor with excellence of their individual skill to find out understanding of *Dosha Dushaya Samurchana* (aetiology and pathology of disease) and *Samprapti Vighattan* (breaking of pathology of disease to get healthy state of functions). Ayurveda viewed health as a state of many-sided equilibrium, and disease as its reversal. Ayurvedic practice of medicine aimed at the restoration of equilibrium and, in that process, represented more than the sum of dietary regimen, procedures and medications.

As quoted in *Chikitsa Chatuspad* after the physician, medicine is said to be the second most important part and it is considered as the main tool by which one performs his duty of treating the patient^[03]. In general we may categorise all Ayurvedic drugs in two group i.e. *Kasthoushadhies* (herbal preparation) and *Rasaoushadhies* (Herbo-bio-mineral-metallic preparation).

Rasashastra may be defined as a branch of *Ayurveda* which deals with the various pharmaceutical processes of

Shodhana (purification/potentiation), *Marana* (incineration/calcinations), *Jarana* (polling), *Murchana* (a procedure by which substances specially mercury is transformed for therapeutic application) and other detail description of metals, minerals, poisonous herbal drugs and animal products used therapeutically in practice of *Ayurveda*.^[04] The innate qualities of *Rasaoushadhies* like quick action, lesser dose, tastelessness, prolonged self life, better palatability have helped conquer the demand of patients as well as pharmaceutical proprietors.^[05]

Ayurvedic Pharmaceuticals:

This review discuss the *Shodhana* (Purification/potentiating) and *Marana* (incineration/calcinations) procedures of Ayurvedic pharmaceuticals which are most relevant to answer queries regarding safety of these *Rasaoushadhies*.

Concept of *Shodhana*:

Shodhana is a process of purification and detoxification by which physical and chemical blemishes and toxic materials are eliminated and substances are subjected for further processings.^{[07][08]}

Procedures of *Shodhana*:

Following procedures are performed for the purpose of *shodhana* as per physico chemical characters of substances.

1. *Abhisheka* (sprinkling) e.g. *Mandura* (Iron oxide) *Shodhana*
2. *Achushana* (absorption) e.g. *Bhallataka* (*Semicarpus anacardium*) *Shodhana*.
3. *Atapa/Agni Shoshana* (drying) e.g. *Shilajatu* (*Black bitumen*) *Shodhana*.
4. *Bharjana* (frying or roasting) e.g. *Gairika* (*Ochre*) *Shodhana*.
5. *Bhavana* (levigation) e.g. *Hingula* (*Cinnebar*) *Shodhana*.
6. *Dhalana* (melting and quenching) e.g. *Naga* (*Lead*) *Shodhana*.
7. *Galana* (melting and straining) e.g. *Gandhaka* (*Sulphur*) *Shodhana*.
8. *Mardana* (trituration) e.g. *Parada* (*Mercury*) *Shodhana*.
9. *Nimajjana* (dipping) e.g. *Vatsanabha* (*Aconitum ferox*) *Shodhana*.
10. *Nirjalikarana* (evaporation of water) e.g. *Sphatika* (*Alum*) *Shodhana*.

* Corresponding author

11. *Nirvapa* (heating and quenching) e.g. *Lauha* (Iron) *Shodhana*.
12. *Parishravana* (straining) e.g. *Navasadara* (Ammonium chloride) *Shodhana*.
13. *Patana* (sublimation) e.g. *Parada* (Mercury) *Shodhana*.
14. *Prakshalana* (washing) e.g. *Godanti* (Gypsum) *Shodhana*.
15. *Prithakikarana* (separation) e.g. *Guggulu* (exudates of *Commiphora mukul*) *Shodhana*.
16. *Swedana* (boiling under liquid bath) e.g. *Sankha* (Conch shell) *Shodhana*.
17. *Vilayana* (elutriation) e.g. *Shilajatu* (Black bitumen) *Shodhana*.

In these processes (of *shodhana*) explained in Ayurvedic classics, very precise approach is employed at each step in terms of equipments, herbal juices/decoction, animal products used in the procedures to fulfil objectives of purification and potentiation.

Concept of *Bhavana*:

Bhavana is a process of wet grinding in which materials are ground with specific liquid media for a particular period to bring minute particles of the material in contact with the liquid media, transformation of the coarse powder to finer state, impregnation of properties of the media to the material which leads to unique and suitable physico-chemical changes i.e. induction of trace elements from herbal juices, to potentiate the efficacy of the material and to facilitate further processing of *Maran*^[9].

Procedure of *Bhavana*:

Required amount of substances and liquid media are levigated smoothly for specific period and is shaped as requirement, often in flat shape and if pressed between finger tips it should be soft to touch, this is considered as indication of proper completion of process.

Concept of *Marana*:

The process which converts the purified metals and minerals into *Bhasma* (fine powder) after subjecting them to levigation and incineration is called as *Marana*.

Procedures of *Marana*:

Purified and detoxified material is mixed with drug for incineration (*Maraka Dravya*) and is levigated with particular liquid media for specific period. Pellets are made from the doughy mass after *Bhavana*. And these pellets are kept in one earthen saucer, allowed to dryness and covered by another earthen saucer and junction is sealed by mud smeared cloth. This *Sarava Samputa* (sealed earthen saucer) is subjected to *Puti* (quantum of heat applied for incineration) for incineration. After self cooling the pellets are collected and ground to powder form. This process is repeated for specified times e.g. *Lauha Marana* (incineration of treated iron), *Abhraka Marana* (incineration of treated Biotite), *Sankha Marana* (incineration of treated conch shell)

The whole process of *Marana* may be summarised as:

Mishrana (Substance) → *Bhavana* (Impregnation) → *Chakrikakaran* (disc formation) → *Samputikaran* (sealing in earthen vessel) → *Shushkana* (drying) → *Putapaka* (heating process) → *Mardana* (grinding) and *Grahana* (procurement of final product).

Observation:

Role of *Shodhana*:

It is very interesting to note that specific media is used for *Shodhana* of eac, like *Triphala Kwath* for *Shodhana* of *Lauha*, *Gomutra* (cows urine) for *Shodhana* of *Vatsanabha*, etc. Sometimes media acts like solvent, to dissolve the material for easy separation from the insoluble impurities as in *Guggulu* and *Navasadara Shodhana*. In some other cases media acts to eradicate toxic chemical substance from the drug e.g. *Manahshila* (native realgar) is found with white arsenic (As_2O_3), which is a highly toxic substance. For *Manahshila Shodhana*, *Churnodaka* (lime water) is generally used because white arsenic (As_2O_3) readily dissolves in solutions of alkalis but realgar (As_2S_2) is insoluble in alkali solutions. Here, *Churnodaka* acts to eradicate highly toxic As_2O_3 from *Manahshila*.

Some materials are used directly in therapeutics after *Shodhana*, wherein media may have some organic and inorganic active principles, which have important role in the body. In addition to these media helps in physical transformation of some metals and minerals. In *Nirvapa* (first immense heating and subsequent quenching in cool liquid) process repeated heating and quenching in liquid media causes brittleness, breaking and size reduction of the metals and minerals.

The objective of these physico-chemical changes of the material is to increase its biological availability, i.e. to potentiate its biological efficacy. Reduction in particle size helps in absorption, smoothness leads to non-irritability, and all chemical changes make the material body friendly like *Shodhita Vatsanabha* (*Aconitum ferox* Wall purified in cow's urine) is converted into cardiac stimulant, where as crude *Vatsanabha* is claimed to be cardiac depressant^[10], seeds of *Kuchila* (*Strychnos nuxvomica* Linn) purified in cow's milk show Central Nervous System depressant activity, pentobarbitone hypnosis potentiation, inhibited morphine induced catalepsy. *Anjana* (*Stibnite/coryllium*) purified in juice of *Bhringaraja* (*Eclipta alba* (L) Hassk) is proved non-toxic to eyes in experimental animals.

Role of *Bhavana*:

Bhavana process increases the therapeutic efficacy of the material. Organic components of the liquid media are transferred to the material to make it organo-metallic or organo-mineral compounds, which are favourable to the body.

Role of *Marana*:

The process of *Marana* is responsible for numerous changes which translate these materials to a magnificent medicine. In brief these are:

- 1-Reduction in particle size
- 2-Conjugation of trace elements
- 3-Elimination of unwanted elements
- 4-Formation of desirable compounds

The objective of the physico-chemical changes is to increase the bioavailability of the *Bhasma* (treated ash as ultimate product of incinerated metals/minerals). Reduction in particle size helps in easy absorption. Formation of desirable chemical compound helps to perform specific therapeutic activity and the trace elements fulfil the demands of trace element in the body^[11].

Quality Control of *Bhasma*:

Generally layman believes that in ancient time, scholars of this branch of knowledge don't have measures for quality control of *Bhasma*. In fact, they had every infinitesimal parameter which may guarantee to consumers about quality, safety and efficacy of products which are discussed here with.

These parameters can be divided into two groups:

(1) Physical parameters^[12]:

To assess the physical properties as lightness, fineness, consistency etc. the following parameters are to be considered as the physical tests.

Varitara (floating of Ayurvedic *bhasma* on water), *Unnama* (ability of *bhasma* to float on water, even after a grain is also put over film formed by *bhasma* over water), *Rekhapurnatava* (particle must be inserted in furrows of finger of human hand to ensure particle size), *Slakshnatvam* (freeness of particles from adhesiveness to each other), *Susukshma* (reduced particle size) test: These tests are applied to study the lightness and fineness of *Bhasma*. And these ensures microfineness of *Bhasma* that will not cause any irritation to mucus membrane when it come in contact.

(2) Chemical parameters^[13]:

To assess the chemical changes as in like compound formation etc. the following parameters are to be considered:

(a) *Varna* :

It indicates the colour of the *Bhasma*. A specific colour is mentioned for each *Bhasma*. And alteration in this specific colour suggests that the *Bhasma* is not prepared properly. Because a particular metallic compound is formed during *Bhasma* preparation and every chemical compound possesses specific colour.

(b) *GataRasatvam*:

Every metal has its specific metallic taste. The properly incinerated *Bhasma* of a metal should be tasteless on taste perception. It indicates transformation of the particular metallic taste to tasteless compounds by unique procedure.

(c) *Nishchandravam* :

The *Bhasma* must be *Nischandra* (lustreless) before therapeutic application. *Chandratva* (lustre) is a character of metal. After proper incineration the lustre of metal should not remain. So in *Bhasma* form, metallic character of the metal should be changed. This test indicates change of the specific metallic lustre to lustreless compound after incineration. This test is applicable to many other metallic and *Abhraka Bhasmas*.

(d) *Apunarbhavata* :

This test is done to ensure that the *Bhasma* is completely formed and it does not come back to its original state (metallic form) when heated along with *Dravaka gana*. *Apunarbhava* means incapability to regain the original metallic form. This test is indicated specifically for metallic *Bhasma*. It reflects the proper or improper formation of *Bhasma*. The properly formed *Bhasma* should not return to its natural metallic form.

(e) *Niruttha* :

Niruttha test is to be considered as inability to regain the metallic form. Because after proper incineration the metal and is transformed to its compounds. So it cannot regain the original metallic form or the same grade of temperature for incineration. This test is applicable to metallic *Bhasmas* only.

Discussion:

Ayurveda is quivering with a novel excitement in its long history. One might even ask, what is the fuss all about? It enjoys the liberal patronage of the Indian State and the recognition of the WHO and developed countries as Complementary and Alternative Medicine. Immensely popular among the people of India^[14]. Although sheltered with long history and high trust, Ayurveda principles have not entered laboratories and only a handful of studies have identified pure components and molecular pathways for its life-enhancing effects^[15].

We illustrate here the merger of Ayurveda and core science in a systems biology scenario that reveals the pathway analysis of crude and active components and inspire ayurveda practice for health benefits, disease prevention and therapeutics.

Credible co-relation with Core Science:

Bearing in mind the above referred concepts regarding Ayurveda, in this review write up a possible co-relation of classical particulars and researches of contemporary time are

discussed. We tried to have pace with recent advances and therefore a primitive theoretical explanation is proposed. Herbo-mineral formulations are here point of magnetism and therefore our first submission that every materia medica of mineral and metallic origin should be established first with geological and mineralogical findings^[16]. Description quoted in current text books of Mineralogy^[17] has distinguished resemblance with description of Ayurvedic and Siddha classics.^[18]

Surprisingly, characteristics features as referred in Ayurvedic classics about these individual minerals and metals have scientific explanation in present day language. *Shabda* (Cry of Tin) may be explained as slip process^[19].

Mardana (grinding with liquid of bhavana) is a process which has been attributed for many exceptional changes taking place in these industrially used material to be used as medicine. This is possible because grinding serves two purposes i.e. produces new surfaces for reaction and provides specified size^[20].

Particular media is mentioned for levigation of specific material indicates some basic relation between the particular media and specific material. Can we co-relate this specifics with organic and inorganic constituents of plant material which may be based on DNA of same and its possible interaction with these minerals and metals on account of adsorption, penetration, absorption and formation of organo-metallic compounds ultimately which is a therapeutic molecule? Studies had established that in aqueous media, interactions takes place and similarly in the kinetic studies of the adsorption processes, different mechanisms for same have been suggested. Use of equilibrium dialysis and electrometric techniques extents of binding of cationic, neutral and anionic surfactants in equilibrium and non-equilibrium states are determined and thermodynamic treatments of the data have been made. Recent extensive developments of these subjects made in the last two decades revealed about possible applications of the topics for industrial applications and understanding of biological processes.^[21]

This research work may lead to new understanding of individualised phenomenon of *Shodhana*, *Bhavana* and *Marana* of Ayurvedic pharmaceuticals in which different aqueous based media is used for desired changes in substances for medicinal use.

These organic materials have basic properties to interact with some specific mineral and metals. Polysaccharides templates are capable to penetrate nanoparticles of iron oxide. Interaction between iron sulfate and template has been carried out in aqueous phase, followed by the selective and controlled removal of the template to achieve narrow distribution of particle size. Particles of iron oxide obtained have been characterized for their stability in solvent media, size, size distribution and crystallinity and it was found that when the negative value of the zeta potential increases, particle size decreases.^[22]

Procedures involved in preparation of *Lauha bhasma* viz *Shodhana* and *Marana* of *Lauha* and *Bhavana* between two *puta* involves very complicated processes in which exposure of many herbal material containing various varieties of diasaccharides and poly saccharides took place along with the heating pattern of *Lauha* for its conversion into medicinal form which is combination of oxides of iron^[23].

Considering these pharmaceutical operations of Ayurveda if we compare and correlate few contemporary research works on same element it looks nearer and complementary to each other. For example as per one research work the unique physical properties (regarding size and shape, magnetic characteristics, biocompatibility, etc.) of magnetic iron colloids in the submicrometric and nanometric size ranges have found increasing and very promising applications in the biomedical field, particularly in drug delivery (Arias et al., 2006). In this work, researchers have synthesized carbonyl iron/CAP core shell nanoparticles for the first time and their dielectric constant and dielectric loss were analyzed in over range of frequencies. Researchers correlated the dielectric measurements with controlled drug delivery. The results of CAP core/shell nanoparticles showed sustained drug delivery compared to pure CAP tablets. It is therefore hoped that with further study, dielectric analysis may become a useful tool for the study of controlled drug delivery system^[24]. In Ayurveda too, *Kanta Lauha bhasma* (compound of magnetic iron) is supposed to show best therapeutic result among all kinds of *Lauha bhasma* and its all pharmaceutical process of its preparation has commendable connection in terms of concept with contemporary researches.^[25]

We wish to quote one more excellent research work which again supports all basic themes of Ayurvedic pharmaceuticals. This paper quote "besides the remarkable therapeutic success of anticancer drugs such as cisplatin, carboplatin and oxaliplatin, metallodrugs have also shown promising results in the treatment of diseases other than cancer. They have been developed to treat/cure a variety of ailments viz. diabetes, ulcer, rheumatoid arthritis, inflammatory and cardiovascular diseases etc. The enzymes in our body and many drugs of organic nature require traces of metal ion for proper functioning. Due to a wide variety of coordination spheres, ligands design, oxidation states and redox potential, coordination and organometallic complexes are supposed to alter the kinetic and thermodynamic properties of the complexes towards biological receptors. Thus, chelation causes drastic change in biological properties of ligands as well as metallic molecules. Metal complexes are supposed to exert their effect by inhibition of enzymes, interaction with intracellular biomolecules, enhanced lipophilicity, alteration of cell membrane functions and arrest of cell cycle etc. The review includes the current use and future potential of some metal based drugs used/showed promising results in the treatment of diseases/conditions such as diabetes, ulcer, infection, mania and hypertension etc. which are being developed as therapeutic agents during the recent past"^[26].

In the vicinity of Nanotechnology:

Ayurvedic *Bhasma* are most ancient illustration of nanotechnology which demonstrated nano particle size in its finished form.^{[27][28][29][30]} How these metals/minerals converted into form of a nanomedicine? Answer is very simple here, this is attribute of classical method of preparation of these *Bhasma* which involves exposure of organic materials with different objectives and heating pattern of all these in a specialised way^[31].

This fact of Ayurvedic pharmaceutics is supported as quoted 'And from time immemorial, Nature has made noble metals part of our daily life. Dendrimers represent a novel category of uniformly sized polymeric molecules, with a regular and highly branched three-dimensional architecture. Dendrimers have been interesting substrates for metal nano particle synthesis, primarily due to their uniform structure and their ability to protect the nano particle surface from agglomeration through the steric effect of the dendritic chain. Biological synthesis of metal nanoparticles reveals the interaction of biological systems with metal ions which is an old subject'^[32].

Proximity to Metallopharmaceuticals:

Metallopharmaceuticals is a term used in conventional system of medicine for the molecules in which metals are prominent in structure and functions. Many researchers are reporting better therapeutic effects through these metallopharmaceuticals.

The redox chemistry of mononuclear and dinuclear gold(I) phosphine arylthiolate complexes was recently investigated by using electrochemical, chemical, and photochemical techniques. Structural and electrochemical differences between gold(I) aromatic and aliphatic thiolate oxidation processes are significant in drug delivery^[33]. Leads to the cellular effects of the anti-arthritis gold complexes may come from the determination of their metabolism by target cells and, possibly, cells in the immediate environment of the target cells.^[34] Considering polymeric drug delivery systems, one may describe the use of synthetic polymers as metal-containing drug delivery vehicles in medicine.^[35]

We will see just how this technology (metallo pharmaceuticals) leads to conjugates distinctly superior in antiproliferative activity to cisplatin, a clinically used antitumor agent used here as a standard. Polymer-drug conjugation involving metal-based and other medicinal agents has unquestionably matured to a practical tool to the pharmaceutical scientist, and all indications point to an illustrious career for this nascent drug delivery approach in the fight against cancer and other human maladies^[36].

Claim with Combinatorial Chemistry:

In future drug development from natural products will not necessarily rely only on the discovery and analysis of new structures from nature's extremely rich biodiversity, but can systematically explore combinatory drug regimes. The introduction of the high throughput-technologies makes this

possible. System biology is evolving as a key discipline to address this task, which is a multidisciplinary challenge still based on experimental biology^[37].

The rate of change of heavy metal ions concentrations in the organism or biological system will determine the choice of strategy of realization of heavy metal ions effect and, consequently, the biological effects itself. Which of the possible strategies will dominate depend on the rate of change of concentration of heavy metal ions in biological systems, functional activities of the organism at the moment of metal action and on metals chemical properties. In the event of slow increase of its concentration in organisms, it produces induction of metallothioneins, other stress proteins and relative changes in the whole metabolic system. This, first of all, results in formation of a new specific epigenotypes, which provides higher resistance (hormesis effects) not only to metal ions that induced this effects, but also to other stress factors^[38].

Equally important is to keep in mind that the end points of toxicity should also be relevant to the exposure of concern and to human health. It became apparent that the concomitant intake of other minerals, particularly calcium, iron and copper, may be a more important determinant of the absorption and toxicity of lead and cadmium than is the co-exposure to Zn, as can be seen in the studies reviewed for this report. For example, data from animal and human studies of Zn(Zinc) and Pb(Lead) suggested that moderately elevated Zn intakes may slightly inhibit Pb absorption and haematological effects in children who have deficient or marginal Zn intakes, but were not adequate for adjusting absorption parameters in the Integrated Exposure Uptake Biokinetic (IEUBK) model for Pb^[39].

These exceptional thoughts of contemporary researches may be a boon for further advancement of Ayurvedic metallic medicines. New thrust area may be developed on these terms for better drugs applying characteristic of combinatorial chemistry.

Recent Researches:

'Garbha Cintamani Rasa' (GCM), used in puerperal complications, is one of unique metallic-herbal Ayurvedic preparation. In this preparation, various roasted metals (*Bhasma*) are used with other medicinal plants. These incinerated metals are found to be chelated with organic ligands derived from these plants liquids. These *Bhasmas* are biologically produced nanoparticles and are taken along with herbal liquids. Thus, this makes these elements easily assimilable, eliminating their harmful effects and enhancing their biocompatibility. This research has shown that GCM improved liver synthetic activity, reduced lipids level and increased kidney function parameters. Diabetic condition alters these parameters specially lipid profile. GCM may be used to improve the complications in diabetic condition. If further investigations show hypoglycemic activity then GCM could be a safe Complimentary and Alternative Medicine (CAM) in diabetic treatment^[40].

Mahamrutyunjaya Rasa (MHR), an Ayurvedic herbo-mineral formulation is used as cardiotoxic. MHR contains potentially toxic compounds like aconitine, which are detoxified during preparation using traditional methods. Any deviation in methods can lead to deleterious effects on human health, so stringent quality control is needed. It is evident from the results that MHR possess significant cardiotoxic property. But, the differences (read two samples) in the results of toxicological and pharmacological studies prove the need of stringent regulatory control over the manufacture and quality control of this Ayurvedic formulation. The alternative medicines in a number of countries have been banned owing to the toxicity due to improper processing of the components and lack of quality control standards. Thus a need arise for the development of reliable standardization tools for effective utility of these traditional medicines^[41].

Mineral arsenicals have long been used in traditional medicine for various diseases, yet arsenic can be highly toxic and carcinogenic. Arsenic in traditional medicine comes from deliberate addition for therapeutic purposes, mainly in the form of mineral arsenicals including orpiment (As_2S_3), realgar (As_4S_4) and arsenolite. Inorganic arsenic is now accepted in Western medicine as a first line chemotherapeutic agent against certain hematopoietic cancers^[42].

Promoting Possibilities:

Many published review attempts to portray the discovery and development of medicine from galenic to genomics, with a focus on the potential and role of ayurveda. Natural products, including plants, animals and minerals have been the basis of treatment of human diseases. Indigenous people derived therapeutic materials from thousands of plants; however discovering medicines or poisons remains a vital question. Considerable research on pharmacognosy, chemistry, pharmacology and clinical therapeutics has been carried out on Ayurvedic formulations. Many of the major pharmaceutical corporations have renewed their strategies in favour of natural products drug discovery and it is important to follow systems biology applications to facilitate the process^[43].

Numerous drugs have entered the international pharmacopoeia through the study of ethnopharmacology and traditional medicine. For Ayurveda and other traditional medicines newer guidelines of standardization, manufacture and quality control are required. Employing a unique holistic approach, Ayurvedic medicines are usually customized to an individual constitution. Traditional knowledge driven drug development can follow a reverse pharmacology path and reduce time and cost of development. New approaches to improve and accelerate the joint drug discovery and development process are expected to take place mainly from innovation in drug target elucidation and lead structure discovery. Powerful new technologies such as automated separation techniques, high-throughput screening and combinatorial chemistry are revolutionizing drug discovery.

Traditional knowledge will serve as a powerful search engine and most importantly, will greatly facilitate intentional, focused and safe natural products research to rediscover the drug discovery process^[43].

Recent developments in computational biology and bioinformatics have provided biologists with some systematic methods to analyze these molecular networks in a cellular context. Collectively predicated as systems biology, it aims to analyze relationships among elements (nodes) in a given system or the emergent properties of the system. Cellular networks that model the cellular response to a given perturbation would include protein-protein interaction networks (PPI: encode the information of proteins and their physical interactions); signal transduction and gene regulatory networks (STN and GRN: show regulatory relationships between transcription factors and/or regulatory RNAs, as well as the signalling pathways that confer these responses); and the metabolic networks (MN: illustrates the biochemical reactions between metabolic substrates and products). Molecular networks that occur in a cell can be presented as either directed or undirected graphs.^[15]

Ayurvedic pharmaceuticals may channelize new drug discovery as suggested by quoted references advocating adoption of system biology along with other branches of science viz chemistry, pharmacology, physiology, microbiology, biochemistry and molecular biology in researches of Ayurvedic drug delivery system.

Global State of Affairs:

In the United States, Ayurvedic medicine is considered a type of CAM and a whole medical system. As with other such systems, it is based on theories of health and illness and on ways to prevent, manage, or treat health problems. Ayurvedic medicine aims to integrate and balance the body, mind, and spirit; thus, some view it as 'holistic'. This balance is believed to lead to happiness and health, and to help prevent illness. Ayurvedic medicine also treats specific physical and mental health problems. A chief aim of Ayurvedic practices is to cleanse the body of substances that can cause disease, thus helping to reestablish harmony and balance^[44].

The acceptance of this classical definition of Ayurveda by NCCAM (National Centre of Complementary and Alternative Medicine), a unit of National Institute of Health, USA provides enough evidence about acceptability of Ayurveda as a system of medicine. UK, Germany, France, Israel, South Africa and Australia are leading countries which recognized Ayurvedic education and practice.^[45]

Regulatory Requirements:

The Drugs and Cosmetics Act, 1940 (section 33 A to 33 N of chapter IV A) and Drugs and Cosmetics Rule 1945 (Rule 150 to Rule 170) are exclusively guiding about manufacturing, sale and distribution of Ayurvedic Drugs. These rules are covering all aspects of quality, safety and efficacy of Ayurvedic medicines. Recently significant analytical test for standard and quality of Ayurvedic medicines (rule 160),

measures of additional rules to regulate Ayurvedic drugs and for manufacturing advancement of these medicines (rule 169) and to cope regulatory demands of export of Ayurvedic medicines, dept of AYUSH, Govt of India notified regulation for self life period of Ayurvedic formulations under rule 161 B. Every foreign country demand data of clinical efficacy of these drugs so rule 170 has been notified to create data for the same^{[46][47]}.

Concepts of permissible limit of heavy metals in Ayurvedic formulations are in practice^[48]. In recent times, Central Council of Research in Ayurveda & Siddha is implementing a national programme under title of National Ayurvedic Clinical Trial project for generation of multi centric data of clinical efficacy of selected Ayurvedic drugs (including herbo-mineral formulations) to support export of these drugs.^[49]

Expert Expressions:

The Ayurvedic drugs produce their effects on the living body through these pharmacodynamic properties. This approach signifies a holistic drug science, which is more nearer to chemistry. However, some drugs used in Ayurvedic possess different dimensions of activity and attribute. The use of metals in therapeutics became prevalent during the middle ages when Rasa Shastra shrouded on the scene. Rasa Shastra is the chemotherapy of Ayurveda where toxicity is a concern for which sophisticated methods of purification were developed and are still in use.^[50]

Ayurveda used extensively minerals and ashed metals as medicine because in contrast to herbal products the mineral products are long lasting and more efficacious. Such preparations become therapeutically more safe and effective when become old. The mineral products when processed with *bhavana dravays* adopt their medicinal properties. These minerals are subjected to various systematic processes of *Shodhana* or purification, *Marana* or oxidation etc. before their induction in medicine. The final products which are in the form of ashes or *Bhasma* and/or organo-metallic compounds, are claimed to be more effective than the herbal drugs and are prescribed in much smaller doses.^[50]

Number of new chemical entities emerging as commercial therapeutic agents from nature has been rather low after the classical period of natural drug discovery. Another area where natural products chemistry played a vital role is the development and marketing of herbal drugs, which are produced, standardized, and clinically evaluated just like the conventional molecular drugs. Natural products chemistry, with its new armamentarium, provide crucial inputs in the development of more therapeutic agents, and is a key player in molecular biology.^[51]

Contemporary connoisseurs are of opinion that these herbo-mineral formulations of Ayurveda are more effective in comparison of only herbal formulations. This is just revalidation of olden golden perception of Ayurvedist

of 08th century and onwards. Natural product chemistry whether it is of herbal origin or herbo-mineral origin is really advantageous for drug development.

Conclusion:

The enormous complexity of human body offers scope to conceptualize its dynamic organization in a number of ways such as structural, biochemical, functional, etc. The conventional western medicine views the body from a structural perspective, whereas Ayurveda, the ancient medical system of India, understands the human body from the perspective of functions/*tridoshas* (*vata*, *pitta* and *kapha*). These different viewpoints of Ayurveda and western medicine have resulted not only in the use of different terminologies and metaphors to explain the human system but also in their different approaches to health and illness^[52].

'I think what we need is not only just a meeting like this, but also a meeting of minds. That is extremely important: creating borderless minds is important, but at the same time breaking borders is important. What is urgently required are change in attitude of scientists, traditional practitioners and industry on one hand, and special policy initiatives by the government on the other. Only then will we be able to create that Golden Triangle' [53]

The essence of this entire elaborative exchange of information is to invite scientific world to work for validation and re-glorification of Ayurveda as it has been previously started by many leading organizations of our country[54][55] with an appeal to more emphasis on Herbo-mineral formulations of Ayurveda as every classic of Ayurveda maintains that Herbo mineral preparations are very safe and essential for treatment of ailing humanity, provided these are produced without compromising the fundamentals of the Ayurvedic pharmaceutical operations of *Shodhana* and *Marana*, specifically.

With all energy, potency and wisdom of our ancient scholars, we submit that these groups of medicines are as superior as it was, even today. It is compromise in fundamental pharmaceutical process with unwarranted variation that is responsible for any side/adverse effect of mineral and Herbo-mineral formulations.

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