



UTILITY OF CONTEMPORARY PRINCIPLES AND INSTRUMENTS OF PHARMACEUTICAL PROCESSING FOR MILLING, DRYING, MIXING IN AYURVEDIC PHARMACEUTICS - A REVIEW

Dr. Prashant Bedarkar*

Assistant Professor, IPGT & RA, Gujarat Ayurved University, Jamnagar.

***Corresponding Author: Dr. Prashant Bedarkar**

Assistant Professor, IPGT & RA, Gujarat Ayurved University, Jamnagar.

Article Received on 02/11/2018

Article Revised on 23/11/2018

Article Accepted on 14/12/2018

ABSTRACT

Pharmaceutical processing (*Samskara*) and their principles are well explored and applied since time immemorial in Ayurvedic pharmaceutical sciences. With change of era one must ripe the benefits of advancement in principles of pharmaceuticals, technology and instrumentation and moreover it is need of time in view of standardization, globalization and industrial manufacture. Contemporary knowledge of principles of milling, drying and mixing and advancement of instruments for the same is necessity of time hence its review has been done from available resources and applicability of related subject in Ayurvedic pharmaceuticals has been discussed. All of the principles, instrumentation may not be applicable and their selective utility as per process and requirement in different pharmaceutico-clinical set up and their motto along with challenges for practical utility have been discussed. It is concluded that, one can ripe benefit of modern technology and instruments of these pharmaceutical operations to extend the horizons of practical utility, augmentation of effect, ease of operation and augmentation of process yield in Ayurvedic pharmaceuticals. Besides this, the knowledge may help in control over these operations leading to precise operation conditions needed for standardization and quality drug production.

KEYWORDS: *Samskara*, pharmaceutico-clinical.

INTRODUCTION

Pharmaceutical processing (*Samskara*) are well explored and applied since time immemorial (vedic era). Advanced medicinal dosage forms (*Bhasma* of *Vanga*),^[1] knowledge of Versatility (omnipresence) of Microbes in universe especially in Pharmaceuticals and measures of sterilization, Pharmaceutical technology and instruments (*Udukhalā yantra*) etc are its proof. Ayurvedic Pharmaceutical sciences is mother and teacher of current Pharmaceutical sciences like Physical pharmaceuticals, Nanotechnology, Biotechnology, Biopharmaceuticals and Pharmaceutical chemistry etc.

Scope of the subject - Knowledge of Current concepts of Pharmaceutical processing may help Ayurvedic pharmaceuticals in enhancement of efficacy of pharmaceutical processing and ultimately therapeutic efficacy. Processes may be involved in development of measure for standardization and increase precision. It may bring ease in Pharmaceutical operation and thus improve practical applicability, increasing utility of pharmaceutical operations.

One must have knowledge of parallel sciences for optimum utilization of knowledge hence here contemporary principles, techniques and machinery for

few pharmaceutical processing (milling, Drying and mixing) and their utility in Ayurvedic pharmaceuticals has been discussed.

Milling^[2]-(Micronization)-Importance - Milling is not merely Particle size reduction, but it results in to characteristics of particle of a powder. Powder may be an important medicament in therapeutic management or useful in Pharmaceutical preparation of others.

Impact of process of milling - Milling has potential to influence Physical Pharmaceuticals of the drug. It can influence characteristics of particles like size, shape, volume/ bulk density and Surface area etc. Other influences of milling are-Homogeneous Mixing, free flow in tableting, drying rate, dissolution, leaching behavior in solvents (*Bhavana*), moisture content, drug to drug physical interaction, rate of chemical reactions, suspension stability, physical stability of product and dose uniformity. It can influence release and dissolution of a drug and thus ultimately can influence absorption (probably Pharmacokinetics ADME) and drug action too. Especially in case of medicinal compounds less soluble in body fluids (saliva, gastric, intestinal, rectal secretions, tears etc). Particle size has great role in absorption of external medicament/aqueous insoluble drugs, external

medicament. A few Ayurvedic solid dosage formulations eg *Ghana* prepared from *Kvatha* are either water soluble or has comparatively more water soluble portion but still many *Rasavarga Dravya* aren't soluble in water (many *Bhasma*) hence less likely to have significant solubility in Body fluids(exceptions). Particle size may be a major determinant for their absorption. Thus controlled particle size reduction is highly needed and most important in case of *Rasushadhi* having less therapeutic index like-*Shuddha Manhashila*, *Shuddha Hingula*, *Shuddha Haratala*, *Naga*, *Tamra*, *Vanga*, *Makshika* etc. It is also very much important in Formulations which are- water insoluble, sensitive in view of untoward effects and not in the form of powder (micronization is an essential step before administration) e.g. *Kupipakva Kalpa*, *Parpati*, *Pottali* etc. It is also important in formulations which are- water insoluble, sensitive in view of untoward effects and which are in the form of powder (further micronization is not an essential step before administration/ use in Formulation)e.g. *Kajjali* etc. Micronization is also important for comparatively safer other *Bhasma* like *Loha*, *Mandura*, *Abhraka Bhasma* etc and hence probably it has been claimed in classics that trituration increases characteristics of a drug under process. It is also important for Other *Bhasma* of *Sudhavarga dravya*, and drugs which are partly water soluble like *Shuddha Gairika*, which inspite of partly water solubility, their solubility may not affect with particle size if given alone, but still it may get altered when in a formulation.

Additional effects/Benefits of milling- Milling helps in removal of excess moisture (provided it should be below 5%), Homogeneous mixing of multiple ingredients.

Challenges- Milling is Still poorly controlled, poorly understood phenomenon and thus it is not a scrubbing particle in the eyes of only Ayurvedic Pharmacist. There is meager basic understanding of mechanism and quantitative aspects of milling. It is experimentally impossible to fracture particles of uniform size to particles of a smaller and still uniform size. Experimental proof of relationship between energy and size reduction is difficult.

Theory of Comminution- Hooks Law-Stress $\propto$ Strain- It is applicable for state of reversible elastic deformation. It states that stress increases with strain during elastic deformation within range of plasticity, hence there is no reduction of particle size and at threshold (yield point), the object doesn't follows this law causing permanent deformation(size reduction). Yield point-every material gets suddenly reduced significantly after specific time of specified protocol of milling. Yield point of (significant increase in product yield at certain time) individual drugs should be calculated. Moisture and heat (in some cases) unduly extends plastic phase of substances thus raising yield point and need of high amount of energy for effective comminution. Hence dryness of substance and maintenance of temperature are desirable. Young's

modulus(slope of linear portion)-expresses stiffness or softness in dynes/ cm.-irreversible plastic deformation. Griffith theory of cracks and flaws-Energy required for comminution is inversely proportional to size raised to some power. Thus more energy is needed for smaller particle size. Kick's Theory- $E=D_1/D_2$ -Energy required for comminution is directly proportional to ratio of Diameter of feed particles to Diameter of reduced particles. Same energy will be required to reduce particles from 1000 microns to 500microns, 500 microns to 250microns and 250microns to 125 microns. For any particle there is minimum energy that will fracture it.

Most of the efficient mills utilize <1% of the energy input to fracture particles and create new surfaces. Rest of the energy is dissipated in (1)Elastic deformation(2)Transport of material within the milling chamber(3)friction between particles and mill (5)Heat (6)Vibration and noise and (7) Inefficiency of transmission and motion.

Milling rate - Mass and size of the particles and the time in the mill affect the milling rate. Manner In which an operator feeds a mill markedly affects the product. For effective milling, rate of discharge should be equal to the rate of feed. In case of Slow rate of feeding, Product is discharged readily. In amount of undersized or fines is minimized. In case of Fast, choaked fed, Material remains in chamber for long and discharge is impeded by mass of material. There is Greater reduction of particle size and it is used when batch size is small. Size distribution and measurement –There is no method of defining irregular particles in geometric terms (statistical methods available). Common methods for size distribution and measurement-Microscopy, Sieving, Sedimentation and others are adsorption, electrical conductivity(for charged and ionic particles-*Bhasma*), light and X ray scattering(SEM, SEM EDAX), permeametry and particle trajectory.

Practical difficulties in standardization of milling of Ayurvedic Pharmaceuticals, especially Kashthaushadhi – In Ayurvedic pharmaceuticals, often different drugs or plant parts (*Panchanga*) are component of a compound formulation, *Panchanga* is poorly explored. There is no data of plant parts and no genuine suppliers are in market. Powder form often drugs are used in coarse (*Yavakuta/ kwathachurna*). There is very poor control over particle size reduction and distribution in product one cannot discard any portion. The nature of drugs is often complex. Even single drug has Different structures (not only whole plant but even same part too) and thus different response to stroke, leading to different particle size. There are difference of opinion in milling of multicomponent drugs, compound powders and compound *Yavakuta Churna* etc. which if milled together lead to non uniform particle size or if mixed after separate milling, still may lead to non uniform mixing. There is sometimes need for milling few drugs along with some another drugs like

Bhallataka being oily and *Sharkara* having tendency for choking and more at high temperature generated due to choking due to softening (plasticity) viciously leading to high yield point and more energy for milling to desired particle size.

Factors to be focused which may influence milling
Drug related factors-Nature of material-nature of drug like therapeutic index (low), hazardous/schedule E₁ drugs, like in case of metal, mineral etc. in view of cross contamination, purity and adverse effects-like *Vatsanabha*, *Kuchala*, *Bhanga*, *Chitraka* etc., Physical nature of drugs Plasticity, hardness etc like in case of metal, mineral which may affect Grindability of a material (expressed in terms of number of revolutions of a standardized Ball mill, required to yield a product of which 80% passes 200mesh screen). Consistency of drug is also important like milling fibrous material is preferred through cutter mill where as friable is milled preferably through hammer mill/ end/edge runner/ball mill. Dryness of drug (Moisture content/hygroscopicity) also influence grindability. 5% moisture hinders size reduction which may change as per remoisture capacity of drug and grindability at different moisture threshold of drug. Indication i.e. use of drug in specified dosage forms should also be kept in mind while milling.

Availability of drug (rare), cost etc. should also be considered before milling e.g. *Nagakeshara*.

Bulk density of drug may also influence distribution when drugs are milled together like drugs with low (*Ushira*, *Kamala pushpa*) and more bulk density (*Chandana*) etc.

Pretreatment of drug may also be needed some times. Very hard drugs- like *Chandana* require prior reduction in disintegrators. Fibrous drugs like *Ushira* should be passed through cutter mill then for fine disintegration in Hammer/ball mill. Sometimes subsequent treatments are also carried out e.g. Repeat micronization of coarsely milled drug after removal of fine through sieving.

Heat unstable compound like escsenceful drugs, finely powdered and or inflammable material (*Manahshila Shodhana*) may need cold jackets surrounding milling chamber and or receiver. Decidation of proportion of *Panchanga* is important for combined milling of different plant parts.

Technical/Instrument related factors influencing milling

- i) Type of milling technique/machinery used,
- ii) Pretreatment of a machine-cleaning,
- iii) Validation-Temperature of inlet and outlet air, temperature of milled material, size reduction performance at different mill speeds, size frequency analysis from each condition of operation and operating specifications.

Milling chambers – Should be made up of good quality (304) to avoid reaction with drug being micronized. Available machines almost all made up of MS. SS have poor friction, abrasion hence rate of milling decreases. Many mills do have serrated plates in casing to facilitate crushing of particles in between casing and blades/hammers. Iron milling chamber may react with drugs (if moist) e.g. *kasisa*, *Triphala*, *Amalaki*, *Kshara*, *Rasaushadhi* leading to cross contamination.

Technician related factors-These are Rate of feed, residual (tailing) drug in machine, rate of milling, duration of milling may influence product.

Method of feeding/milling (all at once together/ separately milled) especially in case of drug having >1 plant parts to micronized/ *Panchanga*/ powder of multiple ingredients.

Other factors to consider -Atmosphere- For hygroscopic material, dehumidified air should be supplied, control of environmental variations during milling and sieving should be done. For thermolabile drugs(or their components) temperature control should be done. Cyclone collectors reduce over heating. In drugs containing thermolabile ingredients, repeated milling can be done to reduce over heating. Post milling treatment/ precautions like cooling, shifting (particle size determination), collection of samples for analysis should also be considered.

Relationship of effect of individual parameter (Drug related, technician related, instrument/technology specific) on size reduction of individual drug should be evaluated and standards in the form of charts should be developed in view of standardization.

Charts-Graphs mentioned ahead may be maintained- Rate of feeding, %yield/tailings, Particle size distribution for individual Drug (especially Raw drugs of herbal origin), with specified conditions. Influence of speed (RPM of rotor), initial size of drug, effect of moisture content on particle size distribution.

Post milling treatment/ precautions-cooling, shifting (particle size determination), collection of samples for analysis should be taken in to consideration in micronization.

Methods of size reduction - Major responsible phenomenon are- 1.Impact, 2.Cutting, 3.Compression, 4.Atrition and 5.Combined Impact and attrition.

Types of mills –There are Hammer mill, Cutter mill (industrial Mixer), (Disintegrator), Ball mill, Fluid energy mill, Roller Mills and others are edge runner and end runner.

Hammer Mill- It has Rotating, movable hammers. Size reduction of 20-40 mesh can be achieved. At high RPM

(Hammer speed of 7600meter/min) all materials behave as if they were brittle. The more thick the screen in milling chamber, the particle size will be less. Speed can not be changed bellow certain level. Speed is usually directly proportional to degree of reduction in particle size. It derives spheroidal particles. It has wide applicability and used for almost all type of material except abrasive ones, for dried material, filter press cakes, ointments and slurries.

Ball mill - There are balls in closed Cylindrical rotating drum, Grinding material are Balls(SS, Porcelin, Teflon etc) and Rods(Rod mill-for more sticky material). As per shape of vessel they are-Tube mill-Length of cylinder is 4 times its diameter and Conical (conical ball mill)-for further more reduction in particle size). Continuous ball mills where product is continuously received at one end through fitted screen. For dry milling moisture % should be <2%.More the density of balls, more is total weight of balls, which produce subsequent more fine product. For optimum milling volume of balls should be 50% (as that of vessel optimum-30-50%).At critical speed (speed at which balls stuck to and move with periphery of cylinder) no grinding occurs. Most mills work better at 60-80% of their critical speed.

Derives spheroidal particles. Critical speed $N_c = 76.6 / \sqrt{D}$, D =Diameter of cylinder hence large cylinder(with more diameter) reaches its critical speed than small i.e. big cylinders will need less RPM. At too slow RPM no grinding occurs. Speed is not proportional to reduction in size. Optimum diameter of ball is approximately proportional to square root of the size of feed. $D_{ball}^2 = K D$ D –Diameter of feed particles. Smaller the ball size it takes long time for size reduction, but it is more fine. Several vessels can also run simultaneously on same platform. It is used for hard and abrasive material, sterilized products like ophthalmic preparations, ointments etc. Wet grinding can also be done in ball mills like for *bhavana* when the product is to intend to be sterile (Ophthalmic, nasal, open wound). *Rasavarga Dravya* can be micronized during *marana* (to minimize contamination).

Cutting mill (Rotary knife cutter) -It has and horizontal rotor with 2-12 rotating knives turning from 200-900rpm. Cylindrical casing holding screen at bottom has several stationary knives. Feed size should be less than 1 inch thick and should not exceed the length of cutting knives. For size less than 20 mesh, pneumatic product collecting system is needed. Many mills usually have cyclone collector. (exhaust fan discharging product to a bag at upper level). Under best operating conditions size limit of rotary cutter is 80 mesh. It derives sharp irregular particles. It is used for tough, fibrous materials and provide successive cutting or shearing action rather than attrition or impact, maximum *kashthashadhi* especially-*Yashtimadhu*, *Sarpagandha*.

Disc mill – Consist of 2 vertical discs, each may rotate in opposite direction (double runner) or only one may rotate (single runner). Disc may have cutting faces, teeth or convolutions. The material is usually premilled to 40 mesh and is usually suspended in a stream of air or liquid.

Roller mills - Consists of 2-5 rollers operating at different speeds. Involves compression and shearing. They are used for ointments, for mixing and trituration of ointments after heating where there is poor control over particle size in final product e.g. *Gandhaka Malahara*, *Gandhakadya malahara*, *Dadruvidravana malahara* etc.

Colloid mill - Consists of high speed rotor(3000-20,000rpm) and stator with conical milling surfaces between which is an adjustable clearance ranging from 0.002-0.03. Rotors and stators may be smooth or rough surfaced. Smooth surfaced facilitates shearing of liquid layer. Where as rough surfaced rotors and stators are useful for fibrous materials. Fibers interlock and clog smooth faced mills. They are used to process suspensions and emulsions. They are not used for dry materials. May be used for *Bhavana* wet grinding- with plenty of liquid to make slurry.

Fluid energy mill-micronizer – Its principle of working is Attrition where high velocity and violent turbulence of air reduces particle size. Air is passed through nozzles at 100-150 pounds per sq inch(psi). Finer particles are collected by cycloning while larger are struck to the walls of milling chamber till further reduction. They are used for more fine reduction, for thermolabile drugs and they reduces particle size to 1-20microns. Their drawbacks are-Needs small batch size, not favourable for bulk Raw material like *kashthaushadhi* and are not economic.

Disintegrator - It is high efficiency impact mill. Hammers are fixed to rotating shaft. They are used for very hard big chunks, Herbal, Wood hearts (*Chandana*, *Agaru*, *Devadaru*, *Khadira*, *vijaysara* etc) Course powder, for formation fine powder from hard structures and for preparation of *Yavakuta*.

Edge runner - These are not designed/used primarily for micronization. Their principle of working is crushing, friction, pressure, abrasion (in case of stone). They are used for fragile/brittle drugs, to micronized Raw/ *Shodhit Rasaushadhi* like-*Hingula*, *Gairika*, *Svarnamakshika*, *Manahshila*, *Hartal*, *Kasisa*, *Tankan*, *Tuttha*, *Sphatika*, *Saindhava* and *Lavana*, *Kshara*, *Rasaushadhies* which are among schedule E1 or potentially hazardous-like, *Manahshila*, *Hartal*, *Hingula*, *Naga*, *Vanga* etc. They may be used to avoid cross contamination as Cleaning is easy. Contact grinding parts could be SS or stone. In case of SS contact part there is no friction, abrasion, only compaction with pressure is principle of grinding and thus should not be used for micronization. In case of stone contact parts of end runner, there is fair friction and

abrasion. They are primarily used for *Mardana* (trituration) and *Bhavana* (lavigation).

End runner - These are not designed/used primarily for micronization. End runner made up of SS could be preferred for more fragile material may be used like, *Tankan*, *Tuttha*, *Sphatika*, *Saindhava* and *Lavana*, *Kshara*. End runner made up of Iron could be preferred for milling of hard substances like *Loha* (Iron), *Abhraka*, *Makshika* etc., whereas end runner made up of Stone are primarily designed for lavigation.

Mixer grinders - Stone pair (Idli mixture grinders) are used for wet lavigation, (wet milling).

Wet milling e.g. in (Ball mill, idli grinder) reduce particle size effectively than that of dry milling which is principle of *Bhavana*.

Milling and Mardana are different- *Mardana* is not merely particle size reduction. There could be several effects responsible for augmentation of properties of drug like-oxidation, neo complexation (reactions in between chemical moieties)-e.g. *Chatuhshashtiprahara Pippali*, *Shodhit Manahshila*, *Shuddha Hingula* (*Vrushya* effect). Many GMP approved Ayurvedic companies use Ball mills for micronization of *Bhasma*. Wet milling and *Bhavana* (lavigation) are different.

One can achieve better, controlled and faster micronization and mixing with modern technology.

We may apply any kind of desired effects like grinding with pressure, abrasion, rupture of cellular structures with more controlled parameters like control of RPM, generated heat etc. This may reduce time required for manufacture like where more than 21 *Bhavana* (frequently around 7 and occasionally 100 or 1000 *bhavana* are also mentioned).

Adoption of modern milling techniques may effectively reduce particle size, achieve better uniform mixing but process of *Bhavana*, *Mardana* expects more effects hence these instruments may be taken help of rather than substitution of ancient procedures with milling by these instruments. Process of *Bhavana* may impart effects of many other processes as part of *Bhavana* like Slow reaction in between chemical components of ingredients, extraction of ingredients, Hydrolysis, oxidation and many more.

Additional milling of *Bhasma* in ball mill after *Bhavana* in edge runner during *marana* may be recommended.

Drying^[3]-(De-moisturization, Descication)-It is removal of liquid from material usually by application of heat and further it's evaporation. Non thermal methods are also used for drying.

Significance of drying-It helps in i) Preservation (inhibits the growth of Bacteria, yeasts and mold), ii) Stability of product (Stabilizes further change in chemical composition of product) and it's iii) Palatability (Bulk reduction, cost of handling, Packaging, transportation, portability).

Principle of drying- Film of the liquid gets form at the material being dried and rate of evaporation of this film is related to the heat transfer.

Drying (heat transfer) can be augmented by Increasing air flow rate (convection), introduction of high temperature radiation source (radiation), reduction in thickness of material or increasing surface in contact with hot surface (conduction) and by increasing air velocity, Dehumidifying inlet air (rate of drying). On the basis of drying behavior solids can be classified as Amorphous, Fibrous or gelateneous, crystalline and granular substances. Gelateneous substances needs more drying as their external surface during drying turns harder by forming tough layer of gelatinous substances, thus hampering release of internal moisture e.g. *Guggulu*, *Arka*, *snuhikshira*, *Niryasa* of *kshiri vruksha*. Amorphous, fibrous need medium duration of drying and structure and physiological activity of these substances gets affected by high temperature and thus requires Low temperature, reduced pressure e.g. Powders of almost all *Kashthaushadhi*. Some substances gets gelatinized during drying like starch solutions e.g. *Guduchi Ghana*. Crystalline substances e.g. *Tuttha*, *Kasisa*, *Sphatika*, *Saindhava*, *Samudra Lavana* gets dried easily. Inorganic, Mineral origin (*Shodhit* or *Ashodhit Rasavarga dravya* only and not all *Rasaushadhi*). Comparatively dries early due to less hygroscopic nature of many drugs e.g. *Hartala* after *swedana*, *Gandhaka* after *Dhalana* etc. and comparatively even *Bhavit Hingula* and *Manahshila* as well.

Methods of drying are- 1. Air and contact drying (under atmospheric pressure)-It is traditional way. Heat is transferred through the foodstuff either from heated air or from heated surfaces. The water vapour is removed with the air. 2. Vacuum drying-Evaporation of water occurs more readily at lower pressures than at higher ones. Heat transfer in vacuum drying is generally by conduction, sometimes by radiation and 3. Freeze drying-The water vapor is sublimed off frozen material. The structure of material is better maintained under these conditions. Suitable temperatures and pressures must be established in the dryer to ensure that sublimation occurs.

Instruments for Drying - Static bed driers - No relative movement of particles, few are exposed to heat. Surface area can be increased by decreasing thickness of the bed. Moving bed dryers-All particles are exposed to heating surface. Fluidized bed dryers- Particles are continuously randomly movable in a stream of hot air. Pneumatic dryers- Improvement of fluidized bed dryers. Each particle is surrounded with envelop of drying gas

comparatively more efficacious. Methods and their Principles of drying- Shade drying is carried out by air currents through radiation. Sun drying in open atmosphere, Pneumatic drying is done with air currents-

Conduction and radiation. Drying in tray, oven, conical drum is carried out by vacuum and in tray and oven, drying is done by conduction and radiation. Freeze driers work by principle of cold vaporization and sublimation.

Table 1: Types of dryers as per operative method Material not agitated.

Static/Movable	Batch type	Continuous type
Static bed system	Tray and Truck dryers, vacuum shelf dryers, freeze dryers	Tunnel dryers, belt dryers, festoon dryers, Drum dryers
Material agitated		
Moving bed dryers-	Vacuum tumble dryers, Pan dryers	Rotary dryers, Turbo tray dryers, Vibrating conveyor dryers, Tower and cascade dryers, screw conveyor dryers
Fluidized bed dryers	vertical dryers	Horizontal vibrating conveyor dryers, vertical dryers
Pneumatic dryers		Spray dryers, flash dryers

Tray and truck dryers - Tray dryers are most common. They are economic, require less maintenance, are easy to handle and operate, Simultaneously many batches of different substances may be dried. They are of Direct and Indirect type. Their efficacy increases with attachment of perforated trays and Vacuum. **Truck dryers** - Trays are kept in trolley. They possess several benefits like Accidental over heating may be overcome, heat contact is reduced, ease and safety of handling, intermittent changing trolleys reduces electricity by evaporation at room environment. **Tunnel and conveyor dryers** - These are types of Tray drier. **Tunnel dryers** - Trolleys of trays are intermittently pushed through drying tunnel by moving chain after loading and unloading trays, **Conveyor dryers** -continuous circulation of trays. **Turbo tray dryers** - Heated with hot air steam at the top of the trolley and dried material is pushed on tray down and newer surfaces are exposed for heating. **Pan dryers**-These are for small batches of pastes and slurries, it contains set of rotating plows in the pan rotating in the pan that revolves slowly scraping moisture laden mass from the wall and exposing drug to newer surfaces. Vacuum dryers-Steam/Vapors generated during drying are continuously removed under reduced pressure by means of a suction machine. The work at low temperature. They are used for drying of Thermolabile drugs, *Gomutra Ghanavati*, during Preparation of Ghana drying at end stage(susceptible for overheating).Fluidized bed systems-Gas is passed through particulate solid (granular) at velocity greater than settling velocity of particles and less than velocity for pneumatic conveying. Air flow pressure is such that particles flow upward and settles down continuously. They are 2-6 fold efficient than tray driers. They are of vertical and horizontal type.

Pneumatic systems- Spray driers: Only liquids, semi liquids (Suspensions, solutions, slurries, thin pastes). Fluid is dispersed as fine droplets in hot stream which are dried in to fine powder and carried by air current and gravity flow in to a collection system. They are of many types. It has different parts like-free delivery system, atomizer, heated air supply, drying chamber, solid gas separator and product collection system. They enable rapid drying, unique form of final product and are used

for drying of Heat sensitive materials. They can be used for changing the physical form of materials-Encapsulating solid and liquid particles. They are useful for granulation for tablets and capsules-Spherical form has better floability. They enable masking of taste, odor may be done.

Applicability in Ayurvedic pharmaceuticals

(Granules of *Kutaja*, *Mamejava*, *Sudarshana Ghana*, *Gomutra Ghana* etc). Particles are dried in seconds and over heating is avoided (less applied temp due to more surface area of fine particles and liquid for encapsulation). Oils can be encapsulated to granules (oil filled globules) and may be administered in the form of capsules. *Bhallataka* oil may be administered in the form of oil filled encapsulated globules filled in capsules. Sustained release formulations may be prepared altering coatings of different pharmaceutical agents with diverse dissolution and disintegration. Formulation with critical issue of drying like *Amalaki Ghana* (*Amalaki Rasayana*, *Rasanjana*, *Krushna Bola*, *Ghana-Guduchi Ghana*) may be dried by pneumatic driers. Sustained release capsules of encapsulated granules *Ghana* of Heat sensitive poorly palatable drugs like-*Shadanga Paniya* can be prepared. For preparation of sustained release capsules of encapsulated granules *Ghana* of Heat sensitive drugs for good taste odour, to treat nausea like-*Hingvashtaka Churna*, *Lavana Bhaskara Churna*, *Ardra khand*. For preparation of sustained release formulations for sustenance of pharmacologic effect (e.g. better control of blood sugars by *Amalaki Rasayana*, *Guduchi Ghana* and control of Blood pressure by *Sarpagandha Ghanavati* throughout night hours). Encapsulation of particles of *Bhasma* with *sahapan dravya* can be done for target organ specific delivery. *Bhavana* is not merely encapsulation. Form of *Bhasma* gets changed.

Freeze Dryers - Principle of working of freeze driers is lyophilization/ drying by sublimation. Heat sensitive products, getting readily oxidized, material to be dried is first frozen (0.0099°C) and then sublimed by heating under high vacuum. Process is carried out at -10 to -40°C . Dried product may be reconstituted with water at

the time of use. Uses-*Hima* formulations, *Arka* may be dried to form granules. Their shelf life may be increased.

Microwave drying - The material itself is heated (rather than being heated externally by conduction, convection or radiation through external source) to dryness with electric filed (movement collisions of ionized and unionized particles due to random electric currents). It is extremely energy conserving and works at lower temperature.

Modes of drying as mentioned in Ayurvedic pharmaceutical sciences

Direct heat contact - *Samskara* like, *Bharjana*, *Swedana* etc. e.g. *Swedana* of *Haridra* facilitates drying.

Indirect heat contact-Drying of *Kashthaushadhi* Raw drugs, Drying in Sun light, *Bhavana* etc.

Without application of heat (or at lower heat) - Drying in Shade-*Amalaki Phalatvak* (Pulp), Moon light (*Chandraputa*)e.g. *Pravalapishiti*.

Peculiarities of drying method of Pharmaceutical formulations in Ayurveda

Drying in sunlight- It may lead to sterilization, reduction of microbial load, UV decomposition of chemicals, neoformation, Electron/ ionic activation by Photons as Photons act as catalyst. It is drying bellow 50°C and above 0°C(except specified methods like Roasting etc), slow and intermittent drying.

Application of drying in Ayurvedic Pharmaceutical sciences- Raw drugs drying-Herbal, Animal origin, mineral origin. *Vatiguti-Bhavana drava*, Final product, *Cchoornakriya*, Tablets-Granules, Punched, coated tablets, *Rasakriya*, *Ghanavati*, *Khandapaka*.

Selective preference of dryers for Ayurvedic Pharmaceutical products

Tray dryers - These may be preferred for drying of *Vati*, *Guti*, Drying of moist whole drugs preferably *kashthaushadhi* (*Pippali*, *Shatavari*, *Amalaki*), *Rasaushadhi*. Drying with tray driers is economic, *Kashthaushadhi* has more Bulk, Raw form, *Rasaushadhi* are easy to get dry, avoiding chances of cross contamination (Non sticky papers may be used on perforated trays).

Pneumatic dryers-Spray dryers - These may be preferred for drying of *Guggulu*, *Ghana* formulations, *Amalaki Rasayana* (*Amlaki swarasa Bhavit churna*), *Churnakriya* of Hygroscopic drugs.

Vaccum dryers(Under reduced pressure)- These may be preferred for drying of fresh essential drugs or their moist powders (Drugs containing volatile active ingredients in significantly more quantity) like *Chandana*, *Jatamansi*, *Musta*, *Kushtha*, *Tagara*, *Vacha*, *Lavanga*, *Dalchini*, *Elaychi*, *Lashuna* etc., They may be

preferred for *Rasaushadhi* like *Pravalpishti*, drugs containing volatile active ingredients in significantly more quantity like *Lavangadi vati*, drugs containing volatile active ingredients in significantly more quantity/highly sticky and become too hard upon drying like *Lashunadi vati*, drugs containing sugar or jaggery like *Talisadi Modaka*, *Vyoshadi Vati*, *Elad vati* etc. They may be used for intermediate complete drying after each *Bhavana* during preparation and at the end in *Kharaliya Rasaushadhi* (especially in large scale batch/ more number of *Bhavana*)-*Gandhaka Rasayana*, *Chandrakala Rasa* etc.

Fluidized bed dryers- Granules for tableting, *khandapaka* (Granules), *Kharaliya rasa* containing Sugar e.g. *Gandhaka Rasayana* etc. They facilitate drying at Lower temperature. Sugar dosen't gets molten or becomes sticky with low temperature, particle size can be well controlled.

Freeze dryers - May be preferred for drying flowers, essenceful drugs, *Amalaki pulp* (therapeutically active significant quantity of thermolabile ingredients)etc.

Mixing^[4]- It is a process that tends to result in a randomization of dissimilar particles within the system or simply combining of two or more than two substances together.

It can be of two Types- 1. Wet mixing-Liquid-liquid mixing or Liquid solid mixing and 2. Dry mixing- Solids Mixing - Main objectives of mixing may be-Physical mixing to homogeneity, to promote the chemical reaction to get uniform product, dispersion of solid in liquid to form suspension or paste and dispersion of 2 immiscible liquids to form an emulsion.

Liquid mixing/wet mixing - Mixing of liquids is done to prepare true solution (by dissolving 2 or more miscible liquids) or emulsions(by dissolving 2 or more miscible liquids). In the laboratory emulsion is prepared by using pestle and mortar and then it is passed through homogenizer to get fine emulsion.

Uses in Ayurveda-liquid-liquid Mixing- *Basti drava*(*Madhutailika Basti*), While preparing *sneha kalpana*-Addition of liquid media like *Gomutra*, Milk, *Kanji*, *Takra*, *Dadhi*, *Dadhiamla*, *Svarasa*, *Mamsarasa*, *Kvatha*, *Yusha*. Mixing of Milk with decoction or water while preparing *Kshirapaka*. *Suuskma kalpana* (Recently invented and traditionally practiced dosage form).

Liquid solid mixing - Mixing of Powders (*Prakshepa dravya*) in trickle (*Chasni*) while preparing *Avaleha* and *Khandapa kakalpana*. Preparation of *Kharaliya rasa kalpa* with *Bhavana*, on the verge of completion of *Bhavana* (especially in case of single *Bhavana*). After completion of *Bhavana* during micronization of *Kharaliya rasa kalpa*. Preparation of *Malahara* like *Gandhaka malahara* etc. Others miscellaneous uses are-

Pinda taila (addition of Wax after preparation of oil, *Mandurakalpa- Punarnava mandura* (Addition of Powder of *Kashthaushadhi*), *Basti drava*, *Mantha*, *Saktu*, *Sahapana of Bhasma*, *Churnakriya* and *Suksma kalpana* (Recently invented and traditionally practiced dosage form, if lavigation is incorporated).

Solids mixing - Mixing of powders-It is used during preparation of tablets, capsules and compound powders. *Suksma kalpana* (trituration of only powders).

Mixing of semisolids - Done for preparing ointments, creams, pill masses and wet mass for granules.

Mixing mechanisms - Mixing could be a resultant of one or more mechanisms cited ahead. 1. Convective mixing-Bulk movement of groups of particles from one part of powder bed to another. Occurs by inversion of powder bed by means of blades or paddles. 2. Shear mixing-When shear forces occur, it reduces the scale of segregation by thinning of dissimilar layers of a solid material. 3. Diffusion mixing-It occurs when random motion of particles within a powder bed causes them to change the position relative to one another. It is produced by any form of agitation of powder.

Physical properties affecting ideal mixing of powders

Particle size-easy to mix powders with similar particle size, Particle shape-Ideal shape for uniform mixing is spherical (mixing of particles ground in cutter mill with that of hammer mill/ball mill), particle attraction (electrostatic forces), material density, proportions of materials-best results can be achieved if mixed in equal proportion by wt/volume. In case of too large difference in proportions then they are mixed in ascending order of their weight (Geometric mixing). E.g. Mixing of *Rasagandha Kajjali* with *Dhatukajjali* or *Dhatukajjali* with rest of the ingredients of *Kharaliya Rasakalpa* which too large proportion as that of *Dhatukajjali* and some miscellaneous-Magnetism, paramagnetism- in case of *Loha*, *Mandura kalpa* may also influence mixing.

Equipments used for Mixing of powders-These are Tumbler mixer-V shaped, Y shaped, Cylindrical etc, Double cone mixer, Agitated powder mixer and Air mixer.

Uses in Ayurveda-For mixing of ingredients of compound *Churna* like *Lavana Bhaskara*, *Hingvashtaka*, *Sitopaladi*, *Pushyanuga*, for preparation of *Lohakalpa* like *Navayasa*, *Saptamruta*, *Vidangadya Loha* etc. and for preparation of *Sukshma Kalpana*.

There could be primary requirement of micronization along with homogeneous mixing like in case of preparation of *Lavana kalpa* like *Narikela*, *Arkalavana*, *Kshara (Vajraka kshara)*, *Rasakalpa (Lokanatha Rasa)* and formulations where *puta* is applied in *Kaparda samputa* etc.

Mechanisms of mixing-In case of Liquid liquid mixing, mechanisms involved are Bulk transport as in case of stirring with spatula, Turbulent mixing in case of Churning, Eddys currents (generation of Irregular strokes with random intensity and at random intervals) in case of churning of *Takra*, *Mathit* etc. Laminar mixing-Streamline laminar flow is frequently encountered when highly viscous fluids are being processed. Stretching of liquid layers is done by interchangeably pouring a mixture of liquids in to vessels from height as in case of Tea, *Sarbat* (*Panaka*). Mechanism of folding liquid layers is applicable by simple circulation of material in a mixer. In case of dissimilar liquids, if mixer employed folds the layers back upon themselves, the number of layers and hence the interfacial area between them, increase exponentially with time. Molecular diffusion is primary mechanism responsible for mixing at molecular level is diffusion resulting from thermal motion of the molecules. Ficks first law of diffusion-Rate of transport of mass (dm/dt) at an interface of area A , is directly proportional to concentration gradient (dc/dx) at interface.

Scale and intensity of segregation-Intensity of segregation is different at different places. After proper mixing, intensity of segregation becomes zero. Scale of segregation is analogous to scale of turbulence. It can be measured in 2 different ways as linear scale or as volume scale. Linear scale may be considered to represent the average value of Diameter of the lumps where as volume scale roughly corresponds to average lump volume. Time dependence-It is not true that mixing for more time will lead to more and proper mixing.

Equipments used for mixing of semisolids - 1. Triple Roller mill, 2. Agitator Mixer, 3. Planetary mixer. Triple Roller mill-Useful for mixing of solid powder in ointment base.

Equipments for liquid-liquid mixing- Impellers- Consists of a vessel and a propeller. The impeller converts the rotational energy of the shaft into a combination of axial, radial or tangential flow, shear and turbulence. They are used to mix fluids or slurry in the tank. On the basis of flow pattern they produce or on the basis of shape and pitch of the blades they are of 3 types- Radial flow impeller, Axial flow impeller and Tangential flow impeller. There is no formula for selecting the optimum impeller design for a particular mixing process and hence logic and experience is needed.

Axial flow impellers - Axial (down and up, parallel to axis of rotation) pumping is an important flow pattern. They impose essentially bulk motion. Propellers are axial thrust-giving elements and are most common type among impellers. They are widely used in a low viscosity, high speed application. They are used for blending, solids suspension, solids incorporation, or draw down.

Common axial impellers-Marine type propellers, Pinch blade turbines, Low mid solidity hydrofoils.

Radial impellers- They discharge fluid radially outward to the vessel wall. They Provide higher shear and turbulence levels with lower pumping, draws the media from the top and bottom. Straight and crossed blades are used commomnly. They are used for mixing of moderately viscous fluids. Unlike axial impellers, radial impellers are commonly selected for low level mixing (known as a tickler blade) or elongated tanks. They do not have a high tank turnover flow like axial flow impellers and are used for high speed.

Tangential Mixing Flow – When tangential or rotational flow dominates it produces a swirling of the tank contents, often with a surface vortex. U-shaped anchor and square blades are used commonly. They are used for for highly viscous fluids-Can work in fluids 1000times more viscous than fluids in which propellers of comparable size are used.

Paddle mixers- Normally operated at low speed 50 rpm or less. Their blades have large surface area in relation to tank. They remain close to the tank wall and effectively mixes viscous fluids or semisolids. Circulation is primarily tangential, but radial and axial flow may persist even after prolonged operation.

Turbine mixers- Blades do not have constant pitch throughout their length. For radial tangential flow-blades are set at 90°. Turbines with tilted blades produce axial motion. They are used for highly viscous fluids-Can work in fluids 1000times more viscous than fluids in which propellers of comparable size are used.

Other liquid-liquid mixers - Air jets-Mechanism of mixing is intense turbulence. Surface jets of air or less commonly some other gas. Liquids of low viscosity are preferred. These are not useful for foaming, volatile liquids.

Fluid jets - Mechanism of mixing is intense turbulence. Liquids are pumped in to the mixing chamber through a nozzle under pressure jet, enabling mixing.

Baffles- Mechanism of mixing is Bulk transport. They have fixed projections at side walls of the mixing tank. Baffle plates are used for proper mixing of fluid from remote areas. Baffle placement largely depends on type of agitator used. Centrally mounted vertical shaft impellers produce tangential flow(manifested as vortex). Only tangential flow is not sufficient for proper mixing and vortex formation can disturb position of impeller. Hence following measure are adopted to achieve better results- vertically mounted Sidewall baffles. Steep spiral baffles along the walls of tank.

Baffling effect can be achieved by-Tilted propellers, changing shape (uneven) of mixing tank.

CONCLUSION

One can ripe benefit of modern technology and instruments of these pharmaceutical operations to extend the horizons of practical utility, augmentation of effect, ease of operation and augmentation of process yield in Ayurvedic pharmaceuticals. Besides this the knowledge may help in control over these operations leading precise operation conditions needed for standardization and quality drug.

REFERENCES

1. Anonymous. Atharvaveda samhita, Mulamatra Gutika, Chaukhambha Samskrit Pratishthan, Dehli, Reprint 2009. kanda 11 Prapathaka 24, Anuvak 2, 8th verse, page 251.
2. Leon Lachman, Herbert Liberman. Industrial Pharmacy. CBS publishers and distributors, New Delhi, Reprint 2010. Pp. 21-45.
3. Ibid.pp.47-65.
4. Ibid.pp.1-19.