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Review Article

INSIGHT OF GOOD MANUFACTURING PRACTICES IN AYURVEDA

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ABSTRACT

Ayurveda is a life science which deals with not just the treatment of a disease but overall well being of an individual as well. The branch of preparation of medicine in *Ayurveda* has been termed as *Bhaishajya Kalpana*. Standard operative procedure has to be followed for the preparation of medicine which ensures the good quality of medicine. WHO has also given a set of legal guidelines that has to be followed for the production of the medicine.GMP deals with all the aspects from collection of raw drug till the dispensing of the finished product. It also deals with premises and equipment to the training and personal hygiene of staff. With the adaptation of the GMP a good quality medicine can be prepared. Good manufacturing practice is essential in present scenario to meet with global standards.GMP has been made mandatory in most of the countries and is a must for the export of the product. Different guidelines have also been specified in GMP for different kind of preparations which has to be followed by all pharmaceutical companies. Though this concept of GMP came into existence recently, the concepts related to this can be found in the literature of *Ayurveda* from collection of raw drug till it is administered to patient. So small insight has been given in this article regarding GMP

Keywords: GMP, Bhaishajya Kalpana, WHO,SOP, Quality.

INTRODUCTION

The good manufacturing practices were first introduced in national aeronautics and space administrates (NASA) in rocket technology, named as zero defect. Later in 1962 U.S Federal Food and Drug act brought an amendment regarding the G.M.P. The first draft of G.M.P was formed by W.H.O in 1968 and later it was followed internationally. In India GMP was introduced in 1988 as an amendment to Drug and Cosmetic rule 1945. In India licences for manufacture of Ayurveda drugs are issued only to such units which fulfil the GMP requirements. GMP regulations requires a quality approach to manufacturing of the product and enabling companies to eliminate or at least minimize instances of contamination, mix ups and errors, which in turn protects the consumer from purchasing a product which is not effective or dangerous. The end point quality testing is insufficient to assure the quality of individual medicine. The assessment of quality at each step of manufacturing process therefore becomes an indispensable aspect.

Ayurveda medicines have been used since Vedic period for the treatment of mankind and play a very important role in treatment of diseases. The production of medicines has a great role on treatment. The medicines have to be prepared with the good quality raw material and proper procedure for the preparation should be carried out so as to give a standard quality medicine. The good outcome will only be found if standard operative procedure has been followed from collection of raw material till dispensing of the prepared medicines and these have been explained under GMP. The GMP (Good Manufacturing Practices)[1] is a set of legal guidelines that have been regulated by WHO (World Health Organization) since 1975. These guidelines aim to ensure that drugs and other pharmaceutical products are safe and effective. Since then, GMP has been considered a seal of quality for pharmaceutical products. Good Manufacturing Practices have been adopted by many countries worldwide and that includes India which is now the second largest producer of pharmaceutical products in the world. A good manufacturing practice (GMP) is a production and testing

practice that helps to ensure a quality product. Many countries have legalized that pharmaceutical and medical device companies must follow GMP procedures, and have created their own GMP guidelines that correspond with their legislation. Failure to follow the GMP regulation may result in serious consequences including recall, seizure, fines, and imprisonment. In Ayurvedic drug manufacturing also, GMP has become mandatory in the recent times. This paper is an attempt to review the implications of GMP and its importance in Ayurvedic pharmaceutical industry

GENERAL REQUIREMENT PERTAINING TO GMP[2]

The Good manufacturing Practices (G.M.P) for A.S.U (Ayurveda, Siddha, Unani) medicines notified under Drugs and Cosmetic Act 1940 on 23 June 2000 and it should ensure that the Raw materials used in the manufacture of drugs are authentic, of prescribed quality & are free from contamination. The manufacturing process has been prescribed to maintain the standards. Adequate quality control measures are adopted. The manufactured drug which is released for sale is of acceptable quality. There are certain other norms which have been explained in the drug and cosmetic act are as follows.

The factory premises and manufacturing plant should have adequate space for[3]:-

1. Receiving and storing raw material.
2. Manufacturing process Areas
3. Quality control section.
4. Finished goods store
5. Office
6. Rejected goods/drugs store

Some other guidelines which have been mentioned under Good manufacturing Practices are[4]:-

1. **Location and surrounding**
   It should be situated and constructed away from open sewage drain public lavatory or any factory which produces disagreeable or obnoxious odor or fumes or excessive soot, dust or smoke.
2. **Building**
   The building should be free from insects/rodents. it must have adequate light and ventilation Floor and wall should not be moist. And it should be according to provision of factory act there should be adequate working space for placement of equipment and materials .it should provided with proper drainage system in the processing area. The Furnace/ Bhatti section could be covered with tin roof & proper ventilation and along with that there should be fire safety measures.
3. **Water supply and Disposal of waste**
   The water used in manufacture shall be pure and of potable quality. Adequate provision of water for washing and Provision for waste disposal should be made properly as per guidelines of pollution control authorities to render them harmless.
4. **Containers cleaning and stores**
   Containers such as bottles, vials and jars are conducted, there shall be adequate arrangements separated from the manufacturing operations for washing, cleaning and drying of such containers. The container should be stored properly in good ventilation. Different storage area should be maintained for Raw material, Packaging material, finished product.
5. **Raw Materials**
   All the raw material should be stored in the raw materials store. The container used for the appropriate containers should be used to protect the raw drugs from microbiological contamination and Proper environmental condition should be maintained so as to protect the raw drug. It should be stored under different categories/ container like the Raw material of metallic origin, Raw material of mineral origin, and Raw material of animal origin, Fresh herbs, Dry herbs and plant parts.
6. **Production**
   Only approved materials are used for the production of product and samples are taken, as appropriate, during and/or after processing, transfer or filling for testing. In addition to Labels are examined for identity before labeling operations to avoid mix-up plus Packages of finished products bear permanent code marks.
7. **Raw material testing**
   Raw material should be tested in Government quality control laboratories. Before the use of drug for production. Along with that procedure of first in first out should be adopted. And Record of receipt, testing and approval or rejection shall be maintained. Plus Raw material container should be labeled as under test, or approved, or rejected.
8. **Packaging materials and Finished goods stores**
   Packaging materials such as bottles, jars, capsules shall be stored properly furthermore All containers and closure shall be adequately cleaned and dried before packing the product. Also Finished goods shall be checked in quality control lab and referred for packing/labeling. And the product shall be dispatched as per market needs.
9. **Working space, Clothing and hygiene**
   Adequate space for orderly placement of equipment to be employed as to facilitate easy and safe working to minimize mix up drugs, raw material. Proper uniform shall be given along with adequate facilities for personal cleanliness along with Provide facilities for keep their personal things. Manufacturer shall provide adequate facilities for first aid and Periodical medical examination of the workers.
10. **Batch manufacturing records, Distribution records**
    Must maintain batch manufacturing record of all types of product.along with List of raw materials, quantities and various tests with record should be maintained.and Record of quality control Plus Record of manufactured drug to finish product. And only after verified and accepted quality it is cleared for sale. Record date, manpower, machines, and equipments should be maintained. Record of sale and distribution of each batch of medicine shall be maintained.
11. **Labeling**
    Check whether the labels of the immediate and outer container bear In addition to the name of the product, the statements of identity and net contents, the name and address of the firm manufacturing the product or

introducing it into interstate commerce. Any direction for safe use of product.

12. **Record of market complaints**
Maintain reports of market complaints received regarding the product. If complaint received should be corrected and prevent recurrence of such complaint. Once in six months report should be submitted to licensing authority.

13. **Quality control**
Each manufacture shall provide facility for quality control in their premises. The quality control shall verify all raw materials, monitor in process, quality checks and control quality of finished product.

Preferably it should have separate expert. It should have following facilities like it should have 150sq area, Raw drugs, reference books, reference samples. Finished product kept for 3 years. Monitor raw drug, semi finished, and finished product. Record of shelf life and storage of drugs. Patent medicine shall provide own specification. Record special procedure of preparation. Standards for identity, purity as given in pharmacopoeias. Raw materials monitored for fungal, bacterial contamination. QC should have one MD (Ayu) degree qualification person.

Table 1: List Of Machinery, Equipment And Minimum Manufacturing Permises Required For The Manufacture Of Various Categories Of Ayurvedic System Of Medicines[5].

Sl. No	Category of Medicine	Minimum manufacturing space required	Machinery/ Equipment recommend
1.	***Anjana/Pisti***	100 sq. feet	Khalva/mechanised/motorised, khalva, end runner/ ball-mill sieves/shifter
2.	***Churna/Nasya Kwatha Churna***	200 Sq.feet	Grinder/ Disintegrator/ Lepa Pulverize/ Powder mixer/ sieves.
3.	***Pills/Vatti/Gutika Tablets***	100 sq.feet	Ball mill, mass mixer powder mixer pill/vati cutting machine, stainless steel trays/ containers for storage. driers/mechanised chattee(for mixing guggul) where required.
4.	***Kupi pakva/ Ksara/Parpati/ Lavana Bhasma satva/***	150 sq.feet	Bhatti,Stainless steel vessels/ flask, Multani matti/plaster of paris,/copper rod, earthen container, muffle furnace(electrically operated) end/edge runner, exhaust fan, wooden spatula.
5.	***Kajal***	100 sq.feet	earthen lamps for collection of kajjal, tipple roller mill, end runner, sieves, filling/packing and manufacturing room should be provided with exhaust fan & ultra violet lamps
6.	***Capsules Ointments***	300 sq.feet	Air conditioner, de humidifier, hygrometer, thermo-meter, capsule filling machine and chemical balance. tube filling ointment mixer, end runner /mill (where required)
7.	***Syrup***	150 sq.feet	exhaust fan fitted and fly proof, bhatti section, bottle washing machine, filter press/grave filter liquid filling tank with tap/liquid filling machine,
8.	***Asava/Aristha***	200 sq.feet	Fermentation tanks containers and distillation plant where necessary.
9.	***Sura/Araka***	100 sq.feet	Distillation plant and transfer pump. maceration tank, distillation plant, liquid filling tank with tap/gravity filter/ filter press, visual inspection box
10.	***Tail/Ghruta***	100 sq.feet	Storage containers, filtration equipment, filling tank with tap/liquid filling machine.

Knowledge/perception of GMP in Ayurveda

Though the concept of GMP came into existence a few decades ago but the same thing has been explained in the books of Ayurveda are as follows:-

a) RASASHALA NIRMANA VIDHI

Regarding the construction of pharmacy our ancient *Acharyas* had good knowledge of pharmacy and they were much concerned about the *Bhesajaghara* that is the place of production of medicine they also had a good knowledge about the place for construction of pharmacy. Various *Acharays* have given their opinion regarding the construction of pharmacy along with qualities of staff required for pharmacy.

Rasa shala nirmana according to *Rasaratna samurchaya*[6] should be devoid of any fear and trepidation and in kingdom where the ruling is done with virtue and honesty, and it should be the house of Lord Shiva and Goddess *Paravathi*, flourishing in a beautiful place and wise person should perform mercurial processes, A beautiful park is made at the entrance of pharmacy and it should have four entrance along with many windows and we find the reference of *Rasamandapa* constructed in the nearest of the pharmacy which is full of abundant of light The *mantapa* should be drumming with sound of drums and bells; *mantapa* should be firm even and shiny like mirror.

Rasashala niramana according to rasa tarangani[7] should have good ventilation and surrounding places should have good water source. It should not be troubled by human being and animals. And a separate section for *Siddaoushada samrakshana* and should be decorate with *chitrapatas* and arrange the different *yantra upakaranas*.

Working area of *Rasashala* as explained by *Rasarathna samuchaya*[8] is the "*Rasabhairva*" should be installed at the eastern side of the pharmacy. Instruments relating to use of fireworks should be at south-eastern region. In southern part

grinding work is done, an arrangement is made for the processes using sharp instrument at south-western portion of pharmacy in western region all kinds of cleaning washing etc is done. In north-western corners for "*vedhankarma*" converting lower metals into gold is carried out at the northern region. In north eastern part arrangement is made for the storage of medicine as well as raw mineral drugs.

Working area of *Rasashala* as mentioned by *rasatarangini*[9] here it has been mentioned that the installation of Rasalinga at east side of *Rasashala*, then arranging the *Puta*, *Kosti* in south-eastern direction, and grinding and pounding in south direction and performance of *Shsatrakarmas* at south western direction performing of washing and cleaning is done in west direction and drying in north western direction and arrangement of different *Yantras* in north directions and stored of prepared medicine in north east direction.

b) Collection of raw drugs[10]

The therapeutic efficacy of any drug depends strongly on the methods followed for its collection and storage. The ultimate aim here will be to obtain the drug in its peak potency level, the time of collection of drug it has been said that the best time for collection is *Sarad rtu* and for drugs of *Vamana* and *Virecana* the best time is *Vasanta rutu* and drug should be collected in the early morning hours and *Ushna veerya* drugs should be collected from Vindhya hills and *Sheeta veerya* from Himalaya mountains and the drugs could be collected in fresh form only.

c) Methods of collection[11]

According to the classical texts in Ayurveda, the drug collection has to be carried out in most methodical and ritual manner. That is in early hour after bath with calm mind the person should pray to lord Shiva facing the early morning sun. Later the drugs situated towards north should be collected. The above concept is essential to have full involvement of the person collecting the drugs

d) Preservation of drugs[12]

Any drug material which is collected should be stored in suitable condition so as to retain the inherent drug properties until the drug goes into a preparation. For this most primary thing which we required will be the suitable containers to store the raw drugs and to protect it from getting infected by insects and pest. So to protect it different drugs should be placed in different area in pharmacy.

IMPORTANCE OF GMP IN AYURVEDA

Although traditional systems of medicine have been recognized and accepted in most countries, efforts to provide validated techniques to ensure the quality, safety and efficacy of products are being developed. The quality of the finished herbal products is largely dependent and influenced by the quality of the raw materials used. Because herbal ingredients are of complex and variable nature, the requirements and methods for quality control of finished products especially for different products has to be tested. Herbal medicines are prepared from materials of herbal origin, which are often obtained from different geographical and/or commercial sources. As a result it may not always be possible to ascertain the conditions to which they may have been subjected. They may vary in composition and properties. Therefore the controls of starting material, storage and processing assume particular importance in the manufacturing process of herbal medicinal products. A poor quality medicine may contain toxic substances that have been unintentionally added. A medicine that contains little or none of the claimed ingredients will not have the intended therapeutic effect.

DISCUSSION

The increasing use of herbal medicines and the growing demand of the global market for such products has raised concerns on the quality and safety of herbal materials and finished herbal products with the respective national health authorities. Unlike conventional pharmaceutical products, which are usually produced from synthetic materials by means of reproducible manufacturing techniques and procedures, herbal medicines are prepared from materials of herbal origin, the procedures and techniques used in the manufacture and quality control of herbal medicines are often substantially different from those employed for conventional pharmaceutical products. Because of the inherent complexity of naturally grown medicinal plants and the often variable nature of cultivated ones, the examples of contamination with toxic medicinal plants and/or plant parts and the number and small quantity of defined active ingredients, the production and primary processing has a direct

Influence on the quality of herbal medicines. For this reason, application of GMPs in the manufacture of herbal medicines is an essential tool to assure their quality. Though the concept of GMP has came into existence a few decades ago but these concepts were followed from the Vedic period and the references can be seen in *Ayurvedic* texts which have given elaborate description about the *Rasashala* and also about the production of medicine

CONCLUSION

Most countries will only accept import and sale of medicines that have been manufactured to internationally recognized GMP certified pharmacies. Governments seeking to promote their countries export of pharmaceuticals can do so by making GMP mandatory for all pharmaceutical production and by training their inspectors in GMP requirements. The basic tenet of GMP is that quality cannot be tested into a batch of product but must be built into each batch of production during all stages of the manufacturing process. It is designed to minimize the risk involved in any pharmaceutical production that cannot be eliminated through testing the final product.

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