**REVIEW ARTICLE: GMP IN OLDEN ERA W.S.R. TO RASASHALA**

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**ABSTRACT:**

Ayurveda is as the nectar of knowledge, a complete and ideal medical science which has acquired different concepts from almost all the philosophies and sects. All the ideas are collected, compiled, evaluated and then incorporated to create integrated approach of human well being and core development. Production of the quality drug is one of these concepts, which is an ongoing need from ancient time. The production of medicine plays a great role on treatment. Medicines have to be prepared with the good quality raw material and proper procedure for the preparation should be carried out to give a standard quality medicine. To ensure this good quality a standard operative procedure has to be followed for the preparation of medicines, which include all the aspects from collection of raw drug till the dispensing of the finished product. And also from proper premises and equipments to the training and personal hygiene of staff all have a great role in this. GMP (good manufacturing practice), a set of legal guidelines given by WHO, deals with all aspects mentioned above. Though this concept of GMP came into existence recently but roots of this concept can be found in the ancient literature of Ayurved. Elaborately this kind of Quality control guidelines was mentioned in Rasashastra & Bhaishajya Kalpana. This is the branch mainly dealing with manufacturing of medicine. Our Acharyas has developed their own guideline for manufacturing quality product, which mainly includes Rasashala nirmana. Rasashala is the place where all kind of Aushdhies (Rasaushidies, Kasthaushidies) were prepared along with Ras (Parad) Sidhhi/Karma. It is described in almost all main texts of Rasashastra. The fundamentals of the Ayurvedic system are essentially true for all ages and so can be easily adopted time after time, century after century. In this paper an attempt is made to show how much today’s GMP is influenced by principles of Ayurved.

**Keywords - Rasashala, GMP, Rasashastra.**

**INTRODUCTION:**

Ayurveda has its strong root in its own basic principles. It made the science to live so long. It is one of the oldest medical traditions of the world. Ayurveda consists of three fundamental principles (Trisutra [1]) viz. Hetu (etiology), Linga (Symptomatology) and Aushdha (therapeutics). It shows Aushdha has equal role in treatment of various diseases or ailments like Hetu and Linga. Aushdha is also placed in the four Chikitsapada[2] by ancient seers.The fame of any medicinal discipline ofcourse, depends upon curability, safety, affordability of the drugs used in that discipline. Keeping this view in mind our Acharyas has developed their own guideline for manufacturing quality product, which mainly includes Rasashala nirmana. Rasashala is described in almost all main texts of Rasashastra. Rasashala was firstly described in Rasendra chudamani [3]. In Rasayansaar Rasayanshala [4] name is mentioned for Rasashala. Rasashala or bhesajagara or Rasayanshala or pharmacy is always expected to be a quite hygienic and workable place with all facilities and follow a preset guideline and regulations for its establishment. In the similar way Acharyas were much more concerned about minutest parts of the bhesajagara/ rasashala. They concentrated on each part including the construction, interior plans and arrangements, appointment of skilled attendants or staff for different sections. Various opinions have given by Rasaacharays regarding the construction of pharmacy along with qualities of staff required for pharmacy. In almost every classical text of Rasashastra usually a separate chapter is devoted in describing building of Rasashala. One can find detail and scrupulous description of the production unit in such texts. In that description right from selection of the place, water facilities, light facility and availability of raw materials, ventilation etc are ideally given. Aslong with accurate and proper thought off directions regarding to various sections,selection of staff and security are also precisely given in different texts.

In the recent times GMP has become mandatory for Ayurvedic drug manufacturing also. GMP for Ayurvedic medicines are separately mentioned in D&C act [5]. These guidelines aim to ensure that drugs and other pharmaceutical products are safe and effective. As mentioned above, Good Manufacturing Practice is a production and testing practice that helps to ensure a quality product. Failure to follow the GMP regulation may result in serious consequences including recall, seizure, fines, and also imprisonment. 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 too. But if deep dig made into literature of Ayurved we just find that there are plenty of texts that are showing same kind of concept, so here a comparative study was done to give an idea about GMP is not a new concept at all, in fact in ayurved our acharyas already set that kind of regulatory guidelines described in various texts complied below.

**Some basic guidelines that are compared:**

1. **Location and surrounding:**

|  |  |
| --- | --- |
| According To GMP | According To Ayurved [6,7] |
| It should be situated and constructed away from open sewage, drain, public lavatory, Away from any factory | miouizns’ks vladqye fuf[kyv©"k/koXkZla¸kqDrk loZck/kkfooftZrs lo©"k/ke¸kns’k |

Here Upavana pradesa (away from city population and pollution,), asankulam (not congested), nikhil aushadha varg samyukta (having various and plenty medicines), sarvabadha vivarjita (devoid of any problem), yaksha, trakshya, saharaksha (most suitable direction for manufacturing), sarva aushadhamaya deshe (having plenty of medicinal plants). This is showing that very precise guideline are given in classics, also resemble to today’s GMP.

2. **Building:**

|  |  |
| --- | --- |
| According To GMP | According To Ayurved [8,9,10,11] |
| It should have adequate provision of light and ventilation. | visf{krk irs|= okr vkri ,o Pk |
| The building used for factory shall be under hygienic condition. | ifo=s] vkradjfgrsns’ks ] n¨"koÆtrs |
| Allow orderly and logical placement of Equipments and Materials | foiqykf£ylkËkukfUork]lo¨Zidj.kkfUork |
| Water system -Water should be pure and of potable quality. | fo'kqËntyjkfgR;s]ty;U='k¨f“rke~ |
| Proper exists should be there. | prq}Zkjkmi'k¨f“rs]Ádkjifj£¨isrsdikVkxZyjf{krs |
| Furnace /Bhatti section could be covered by tin roof | ,dr¨ “zkf"Vªdk dk;kZ r`.kkPNknuoftZrk |

As above similarities in Ras text there are some more arrangement are given like chatur dwaropashobhite/ Chatusanjavnopeta [12] (having four doors) this can be considered as fire exit too, aatanka rahita deshe i.e. free from violence either animal or human or free from diseases.

3. **Warehousing and stores**

|  |  |
| --- | --- |
| According To GMP | According To Ayurveda [13.14,15] |
| Different storage area should be maintained for Raw material, Packaging material and Finished product. | तत्र शाला----कुटनक्वाथनाद्यर्थ स्थानानि तत्र कल्पयते |
| Containers such as bottles, vials and jars are properly washed, cleaned, and dried. | सुदृढ़ा विविधाकाराः कूपिकाः कांचनिर्मिताः सपिधानाः |
| Good quality raw material should be selected and Protected from microbial contamination. | जन्तुवह्निहिमव्याप्ता नौषध्वः कार्यसिधिदाः| |
| Access to these areas and materials shall be restricted. | सुगुप्ते, जनबाधारहिताम् |

4**. Production area**

|  |  |
| --- | --- |
| According To GMP | According To Ayurveda [16,17,18] |
| Production area should be In order to avoid the risk of  cross –contamination,  Separate dedicated,  Self – contained facilities shall be made available. | vkradjfgrsns…ks] n¨"koÆtrs] i'kq;«k u fo|rs  lqxqIrs lq"kesLFkkus ]'kkafrfujkins ]  uxjL;k··fonq;sZ.k] tuckËkkjfgrkeladqyke~  le`Ënsuxjs]yH;rs nzO; lokZf.k  oiqykf£ylkËkukfUork]lo¨Zidj.kkfUork |
| The manufacturing area shall provide adequate space for orderly placement of materials and equipments, which facilitate easy and safe working. | lqfoLrh.kZk eu¨jek]fotusLFkkus |

5. **Quality control**:

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| --- | --- |
| According to GMP | According to Ayurveda [19,20] |
| Quality control section shall have a separate expert for all manufacturing process. | आचार्यो ज्ञानवान् दक्षोरसशास्त्रविशारदः ----  कुशलो रसकर्मणि | |
| For identification of raw drugs reference books and other scientific books should be maintained. | तेषामेवान्तिके स्थाप्या ग्रन्थाः |  वेदग्रंथोत्तरे |
| Separate air handling units, airlocks and other ventilation requirements shall be provided for quality control laboratory. | visf{krk irs|= okr vkri ,o Pk |
| Quality control section will have a minimum of – a) expert of Ayurved  b) Chemist  c) botanist  d) microbiologist | In R.R.S. 4 types of Parichark(specialist) are mentioned- रसवैद्य  धातुवाद  भेषजाहृतौ  निधिसाधक/बलिसाधक |
| Personnel- personnel for quality assurance and quality control operations shall be suitably qualified and experienced. | रसचिन्तका वैद्या निघंटुज्ञाश्च वार्तिकाः |  सर्वदेशजभाषाज्ञाः संग्राह्यास्तेऽपि साधकैः || |

Here we can see in both guideline section wise specialist appointment is mentioned, which show close resemblance of GMP guideline with Rasa classics. Other than above similarities Acharyas also mention to maintain the quality by collection of raw drugs in respect of that seasons like- they use to collect the herbs in sarada ritu for all types of preparation. For the drugs of vamana & virechana they told to collect in vasanta Ritu. They also mentioned the specific time for specific plant part like Mula has to be collected in Shisira and Grisma ritu etc because of to get the maximum potency from those parts of herbs. Acharaya Sarangadhara also mentioned that place of drug collection as well as place from where drugs should not be collected to maintain the quality of the medicine. He also mentioned that state of drug collection like which should be used in Purana state are Vidanga, Pippali, Madhu etc.

6. **Working Space/Area division**:

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| --- | --- |
| According to GMP | According to Ayurved [21,22] |
| Sections are divided-  Grinding Section | ik"kk.kdeZZ (nf{k.kkfn'kk) |
| Furnace Section | अग्निकर्म (आग्नेय दिशा) |
| Processing Section | शस्त्रकर्म (नेॠत्य दिशा)  क्षkलनादी कर्म (पश्चिम दिशा)  वेध कर्म (उत्तर दिशा ) |
| Drying Section | शोषणकर्म (वायव्य दिशा ) |
| Finished Goods store | सिद्ध वस्तु स्थान (ईशान दिशा) |

Working area in Rasashala is specifically divided as per direction e.g. the operations related to the use of fire are advised to be carried out in ‘Agnikona’ (South east direction) which is considered to be ruled by God Agni who by virtue of his being the God of fire keeps control on fire related works. The **‘**Nairitya Kona’ **(**South west direction)is advised for performing ‘Shastra Karmas’ like cutting and slicing etc. As this direction is ruled by Raksasas (Demons) who are cruel in nature and keeps the control on sharp weapons /instruments. Hence the cutting, slicing etc. operations involving the use of sharp instruments done in this direction may likely to be completed safely and successfully.

The Varuna kona (western part**)** of the factory is advised for washing, cleaning etc. works involving the use of water. As this direction is ruled by God ‘Varuna’ who is considered to be the God of water resources, so the operations involving the use of water if done in this direction will never face water shortage.

The Vayavya Kona (North West directions)is ruled by the God vayu,who is supposed to control wind. The Uttara digbhaga (Northern part)is governed by God Kubera who is the God of ‘wealth and finances’. Hence the Vedha Karmas(Transformation operation of lower metals into higher metals) are advised to be done in this direction. The Isana Kona (North eastern direction)is ruled by **Lord Siva/rudra** who is the creator of mercurial operations. The transformed mercurial products and the other finished products if stored in this direction then their potency and effectiveness will be preserved for long time and there self life will be prolonged. There is no need to wonder about why such peculiar arrangement is advocated, because all the Ancient sciences from India have religion and God as their base. Rasashastra is also no exception to it. Therefore we can conclude that the objective of such arrangement was to made separate section for each process. In present time the places for each process are also fixed as per availability of water, light and space.

7. **Health, clothing and sanitation**:

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| According to GMP | According to Ayurveda [23] |
| Proper uniform shall be given uniform shall also include cloth, covering for hands, feet and head wherever required**.** | सोद्यमाः शुचयः शूरा बलिष्ठाः परिचारकाः |
| Should be free from contagious disease. |
| Shall be trained in practices. |
| Provide facilities for keep their personal things.  Adequate facilities for personal cleanliness. |

In Ayurved there is a clear mention that workers(Paricharka) must be healthy (balistha)and clean(shuchi). Workers should be pathyashin( i.e. they should consume healthy diet) which keep them away from the diseases. In rasayan sar [24] it has been mentioned that in the premise there should be adequate area for rest, refreshment, toilets as well as for keeping their belongings.

8. **Sanitation In the manufacturing Premises**:

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| --- | --- |
| According to GMP | According to Ayurveda [25] |
| The manufacturing premises shall be clean and maintained in an orderly manner. | शालासम्मार्जनाद्यं --- |
| Specific Areas to be cleaned in particular cleaning intervals. Personnel assigned to and responsible for the cleaning operation. | प्रत्यहं कारयेधीमान शालायां मार्जनादिकम्  भृत्यैः कर्मसु निष्णातैः सदाऽऽतंकनिवृतये |

In addition to that in rasashastra text, a special area known as Rasmandap was described which is basically a very clean and arranged yagya sthan surrounded by bheri mridnga etc. musical instruments and flowers. In this Rasmandap yagya performed on daily basis. Yajurveda advocates performing yagya every day in the morning and evening to attain spiritual enlightenment, mental peace, purification of the mind and environment. Smoke produced from natural substances has been used extensively in many cultures and famous ancient physicians have described and recommended such use. [26]Under the Saraswati-Indus civilization 7500 BC, the great Rishis (saints) used to perform agnihotra-yagnas to purify the environment as described in Rigveda-the most ancient compilation of knowledge on earth by sublimating the Hawan samagri (mixture of wood with odoriferous and medicinal herbs) in the fire accompanied by the chanting of Vedic mantras described in Rigveda. The sublimated vital elements and herbal medicines inhaled in Yagya first reach the brain, followed by lungs and other subtle components of the body. To know importance of Yagya on environment a study carried out by a team of scientists at National Botanical Research Institute (NBRI) which has claimed that smoke emitted during havans(Yagya) reduces airborne bacteria to a large extent, minimizing possibility of infectious diseases.  Here we can explain how sanitation of manufacturing unit was performed in ancient time.

9. **Equipment :**

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| According to GMP | According to Ayuveda [27,28] |
| Suitable equipment either manually operated or operated semi-automatically or fully automatic machinery shall be made available like crushing, grinding, powdering, boiling, mashing etc. | द्रोणीरूपा वर्तुलास्च------शालायां मार्जनादिकम् |
| These equipments have to properly installed and maintained with proper cleaning. | प्रत्यहं कारयेधीमान शालायां मार्जनादिकम्  भृत्यैः कर्मसु |

General equipment like Koshtis, Storage Tanks, Bhastrikas(bellows) ,Mettalic and Bamboo pipes, Vessels and utensils of different size (Gold, Iron, Copper, Bronze, leather and stones), Different types of kandani(small pounder), Peshani(Bigger,flat stone for rubbing), Droni(Big cauldron), Mortars and pestles of different kinds, Taptakhalva etc. and Fuels as Shikitra , Changana, tush, trina are maintained regularly in the Rasashala. In Ras taringini it is clearly mentioned that workers should be appointed for proper cleaning and maintenance of all equipment on daily basis.

10. **Quality Assurance**

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| According to GMP | According to Ayuveda |
| An appropriate quality assurance system should be applied in the manufacture of medicines by the use of modern analytical techniques e.g.HPTLC,GC,CE,AA etc | Quality testing will be carried out as per rasashastra literature -color, taste varitaratwa, rekhapurnatwa, Laghutava etc. bhashama Pariksha . |

In older as well as modern era testing for quality is elaborately given. The quality control parameters in Ayurved were not in terms of a standard numerical value but Acharyas were very well aware of the quality and hence mentioned about dravya sangrahana and dravya samrakshan vidhi which assured good quality. According to different medicines type in Rasashastra texts there are different Parameters to assure quality like for bhasma various kind of bhasma pariksha which provide knowledge about their physical and chemical properties e.g. varitaratwa, rekhapurnatwa, and proper gandh varn uttpati for sneha and sandhaan kalpna etc.

**DISSCUSSION:** It is the duty of scholar to bring out the truth, which is collected in the ancient treatise. In this aspect the Uha or discussion becomes a necessary part of any research work. As per few previous review article [29] and above comparison we can say that GMP( Good Manufacturing Practice) is a very essential part of a drug production. There must be some regulatory guideline that should be followed from collection of raw material to the preparation of a finished product along with premises and choice of staff. After considering importance of all these points Acharyas have mentioned all above rules and guidelines. These are compiled in many Rasashastra related texts and Samhitas. In Rasayansaar elaborative description of Rasashala with proper explanation has been given. This book has been started by importance of Rasashala[30] “Vinaadharm kriyaa kachit sidhhinayaati kahirchit.” Here an effort has been made to recollect and compile these guidelines of Aushadh Nirmana, as a short old GMP source.There are many similarities between GMP and Rasashala but GMP gives some additional points to cover like documentation, record maintaining, product recall etc.We can say these points/rules were generated for industrial production. In ancient time medicine were prepared for limited use and storage. It was not meant for long time or large investment so the present guidelines are the demand of current time where medicines are to be prepared for mass production. Documentation is an important point of GMP which should be followed for all kind of production either it’s for small pharmacies or industrial level, which was not included in Rasashala but separately described according to formulation e.g. in Panchvidha kashay kalpna for each kalpna proper instruction about manufacturing, Jala, Agni parmana , Parkshep Parmana , dose , administration time and other relating points are given in texts. But not separately define like GMP. The principle necessary for quality drug production are scattered in Ayurved classics especially in Rasashastra, we can say these are the olden era’s GMP. Still all the important points of Rasashatra classics cannot be compared but they have their own uniqueness. Ayurved is a treasure of knowledge, and there are still many gems, yet to be explored.

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