## Unit-5

### (A) General Introduction to Herbal Industry

Herbs have been known since the era of civilization & are highly esteemed all over the world as a rich source of medicinal agents.

The herbal industry is a very fast growing sector in the International market. In India, various System of medicine like AYUSH are being utilized for health care of people.

→ Present scope of Herbal Drug industry –

∴ Indian Scope of Herbal Drug Industry :

Herbal drug constitute a major share of all the officially recognized System of health in India (AYUSH) except allopathy.

More than 70% of India's 1.1 billion population still use these non-allopathic System of medicine.

Currently, there is no separate category of herbal drug or dietary supplement as per Indian drug act. However, there is a vast experience-evidence base for many of the natural drugs.

In India, raw drugs obtained from around 2,400 plant species. It is the fastest growing market & may attain to 14,500 crore & export to 9000 crore with a CAGR of 20% & 25% respectively.

The herbal industry has revealed currently that the Indian herbal market size is estimated at 7000 crore & over 5000 crores of herbal raw

material & medicine are exported by India.

In India, there are about 600 medicinal plants are used. Out of which 25 manufacturers are large scale manufacturers. The annual turnover in India was around US 300 million dollar for Ayurvedic & US 27.7 million dollar for Unani medicine.

## International Scope of Herbal Industry :

Acc. to WHO, approx 25% of modern drug used in united States have been derived from plants. More than 120 active compounds isolated from higher plants are widely used in modern allopathic medicine today & 80% of them show a positive co-relation between their modern therapeutic use & traditional use of plants from which they are derived.

Atleast 7000 medicinal compounds from plants, the ingredients of herbal medicine are included in modern pharmacopoeia of drugs.

WHO estimates that 80% of world's population currently uses herbal medicine for some aspects of primary health care. They are also highly demanded in international market, generating billions of dollars in revenue.

To cite of few example, annual revenue from herbal medicines & herbal products in western Europe reached US Dollar 5 billion in 2013-2014.

In China, sales of herbal products reached US dollar 14 billion in 2015.

Herbal medicine revenue on Brazil was US dollar

160 billion in 2017.

→ Future prospects of Herbal Drug Industry –
Herbal medicine based on traditional medicinal system of treatment is a rapidly growing healthcare system of economic importance & is now widely used in many countries of the world.

∵ Phytochemistry : The interest of natural product as a source of new biologically active compounds has expanded due to increasing research & development in phytochemistry. Various phytochemicals are isolated from Herbal drugs & used in the treatment of various diseases.
eg - Quinine isolated from Cinchona is used in the treatment of Malaria, vincristine & vinblastine isolated from Vinca is used in the treatment of Cancer.

∵ Plant Biotechnology : By using biotechnological approaches in plants various herbal drugs are prepared that have valuable impact in the medicinal field.
eg - Edible vaccine are prepared in vegetables & fruits, Enzyme production by fermentation, production of antibiotics

∵ Molecular Biology : With the development in the technique of molecular biology there has been an ↑se of interest in the use of naturally occurring protein as potential therapeutic agent.

∴ **Genetic Engineering :** Several genetically engineered natural product have a significant impact & more than 20 biotechnology derived products are now in market. eg- Tissue plasminogen activator is used as thrombolytic after myocardial infarction, erythropoietin is used to treat anaemia associate with renal failure.

∴ **Modern Herbal formulation :** Now, various modern herbal formulation like solid, liquid, nanoparticles, colloidal, particles, micelles, etc. of herbal drugs are available in market. There is a good scope of modern herbal formulation for future industry.

∴ **New leads :**

The following leads & development are the future prospect of herbal drug industry. Plant products are useful as starting material for semi-synthetic prep$^{n}$ of drugs like Plant steroids (diosgenin) : oral contraceptive & hormone, Microorganism (Streptomyces genus) : Antibiotics (streptomycin)

→ **Overview of plant based industries & institution involved in work on Medicinal & Aromatic plant of India –**

Government of India has expressed support & encouragement for Traditional Indian Medicine (TIM). A separate department for Indian system of medicine & homeopathy now known as AYUSH was established in March 1995 to promote Indigenous system.

In year 1969, the Indian government established a Central Council for Research in India Medicine & Homeopathy (CCRIMH) to develop scientific research in herbal products expanded various government & private research centres developed which are actively engaged in the Research & Development of Herbal Medicines.

## List of Few Research Institution engaged in research in Medicinal & Aromatic Plant of India :-



| S.No. | Name of Institution | City |
|---|---|---|
| 1. | CCRAS (Central Council For Research in Ayurveda & Siddha) | New Delhi |
| 2. | ICMR (Indian Council For Medical Research) | New Delhi |
| 3. | NMPB (National Medicinal Plant Board) | New Delhi |
| 4. | CCRUM (Central Council For Research in Unani Medicine) | New Delhi |
| 5. | NISCOM (National Institute Of Science Communication) | New Delhi |
| 6. | IHMMR (Indian Institute of History of Medicine & Medicinal Research) | New Delhi |
| 7. | NBRI (National Botanical Research Institute) | Lucknow |
| 8. | CIMAP (Central Institute For Medicinal & Aromatic Plant) | Lucknow |
| 9. | CDRI (Central Drug Research Institute) | Lucknow |
| 10. | NIA (National Institute of Ayurveda) | Mumbai |
| 11. | Zandu Foundation | Mumbai |
| 12. | RRL (Regional Research Laboratory) | Jammu-Tawi |
| 13. | Gujarat Ayurveda Pharmacy | Jamnagar |
| 14. | National Institute of Ayurveda | Jaipur |
| 15. | Arya Vaidya Shala | Kottakal |
| 16. | Interdisciplinary School of Health Service | Pune |
| 17. | Banaras Hindu University | Varanasi |
| 18. | RMRC (Regional Medical Research Centre) | Belgaum |
| 19. | PERD (Pharmaceutical Education & Research Development Centre) | Ahmedabad |
| 20. | IMPCOPS (Indian Medicinal Practitioner Co-operative Pharmacy and Stores Ltd.) | Chennai |
| 21. | IMPLANT Centre (Inter-University Medicinal Plant Laboratory For Analysis, Culture & Therapeutic Centres) | Rajkot |

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| Sno | Name of Herbal Drug Industry | City |
|---|---|---|
| 1. | The Himalaya Drug Co. | Mumbai |
| 2. | Charak Pharmaceutical | Mumbai |
| 3. | Zandu Pharmaceutical Works Ltd. | Mumbai |
| 4. | Shri Dhootapapeshwar Ltd. | Mumbai |
| 5. | Biocon India Pvt Ltd. | Bangalore |
| 6. | Cipla Research Centre & Factory | Bangalore |
| 7. | Sri- Sri Ayurveda | Bangalore |
| 8. | Auen laboratories Pvt Ltd. | Kolkata |
| 9. | Herbo-Med Pvt Ltd. | Kolkata |
| 10. | Basic Ayurveda | Ghaziabad |
| 11. | Dabur India Ltd. | Ghaziabad |
| 12. | Acis laboratories | Kanpur |
| 13. | Herbals (APS) Pvt Ltd. | Patna |
| 14. | Shri Baidyanath Ayurved Bhawan | Patna |
| 15. | Shilpachem | Indore |
| 16. | Hamdard (WOKF) laboratories | Delhi |
| 17. | Vico laboratories | Nagpur |
| 18. | Nagarjuna Herbal Concentrates | Kerala |
| 19. | Sandu Pharmaceuticals Ltd. | Goa |
| 20. | Patanjali Ayurveda. | Uttarakhand |

## (6) Schedule T- GMP of Indian System of Medicine

→ Objectives -
The objective of GMP are as followed:

(a) Raw materials used in the manufacture of drugs are authentic, of prescribed quality & are free from contamination.

(b) The manufacturing process is as has been prescribed to maintain the standards.

(c) Adequate quality control measures are adopted.

(d) The manufactured drug which is released for sale is of acceptable quality.

(e) To achieve the objected listed above, each licensee shall evolve methodology & procedures for following the prescribed process of manufacture of drug which should be documented as a manual & kept for reference & inspection.

However, under IMCC Act 1970, registered vaidyas, Siddha, Hakeems who prepare medicine on their own to dispense to their patients & not selling such drugs in the market are exempted from the purview of GMP.

→ Component of GMP -
The GMP are prescribed as follows in Part I & Part II.

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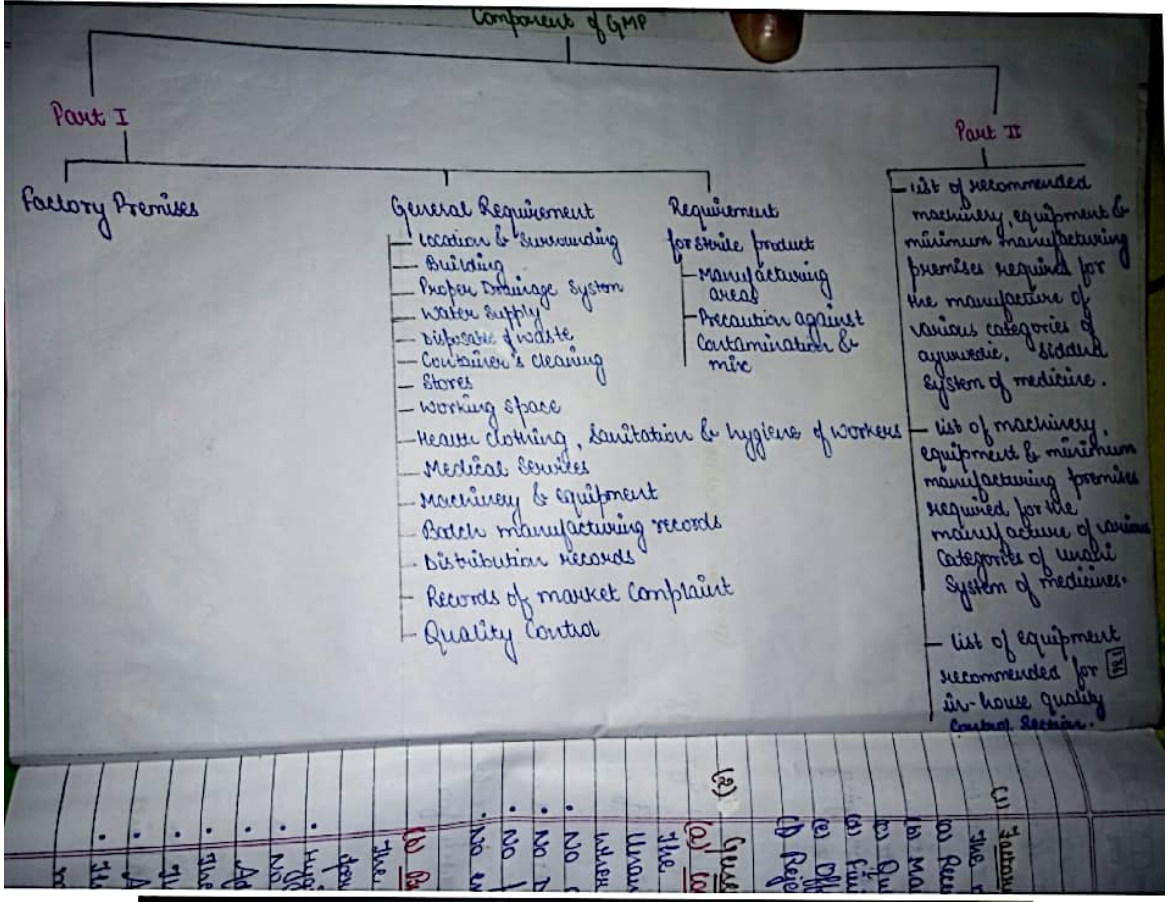


Part - I

(1) Factory premises :
The manufacturing plant should have adequate space for:
(a) Receiving & storing raw materials.
(b) Manufacturing process area.
(c) Quality Control Section.
(d) Finished good store.
(e) Office.
(f) Rejected goods/ drug store.

(2) General Requirement:
(a) Location & Surrounding :-
The premises for manufacture of Ayurveda, Siddha, Unani medicines should be located & surrounded where there is :
- No open sewage.
- No Drainage coming from public areas & toilets.
- No factory fume.
- No excessive soot, smoke, dust.

(b) Building :-
The building should be compatible with manufacturing operation & located where:
- Hygienic Condition are maintained.
- No cobwebs / insects / rodents are present.
- Adequate light & ventilation are available.
- The floor & walls are free from dampness & moisture.
- The floor & walls are even.
- Adequate working space is available.
- The equipment is placed such that the risk of mixing, cross-contamination, risk of omission of

a control step can be avoided.
- The premises are so designed, constructed & maintained that insects / rodents cannot enter.
- The interior surface is smooth, easy to clean & disinfect.
- Flooring is smooth & even to prevent retention or accumulation of dust or waste products.
- The premises for manufacturing, processing, packaging & labelling processes are compatible with the Provision of factory act.

(c) Proper Drainage System :-

The drainage system of the premises should:
- Have proper sanitary fittings & electrical fixtures for safety.
- Have furnace / [illegible] section covered with tin roof.
- Have proper ventilation / chimney in factory.
- Prevent files / dust in factory premises.
- Have proper fire safety measures / exists installed.

(d) water Supply :-

The water used in manufacturing shall be pure & potable quality. Adequate provision of water for washing the premises shall be made.

(e) Disposable of waste :-

The waste water & other residues obtained as by-products of the manufacturing processes & laboratory operation are harmful to work & public health & thus should be disposed after proper treatment as described in the guidelines issued by the Pollution Control Board.

(f) Container's Cleaning :-
There should be an area for cleaning of the containers used in the manufacturing processes. These containers should be washed, cleaned & dried properly.

(g) Stores :-
Storage should have proper ventilation & shall be free from dampness. It should provide independent adequate space for storage of different types of material such as raw material, packaging material & finished products.

# Raw Material :
All raw materials procured for manufacturing shall be stored in the raw material store.
While designing such containers, cabins or areas in the raw materials store, care may be taken to handle the following different categories of raw materials:

- Raw material of metallic origin.
- Raw material of mineral origin.
- Raw material from animal source.
- Fresh herbs.
- Dry Herbs or plants part.
- Excipient, etc.
- Volatile oil/perfumes & flavours.
- Plant Concentrates & excudates/resins.

Each container used for raw material storage shall be properly identified with the label which indicates name of the raw material, source of supply & will also clearly state the status of raw material such as 'under Test' or 'Approved' or 'Rejected'.

# Packaging Material :

All packaging materials such as bottles, jars, capsules etc. shall be stored properly. All containers & closures shall be adequately cleaned & dried before packing the products.

# Finished Products :

The finished goods transferred from the production area after proper packaging shall be stored in the finished goods stores within an area marked 'Quarantine'. After the QC laboratory & the excepts have checked to the correctness of finished goods w.r.t its packing / labelling. as well as finished product quality as prescribed then it will be moved to 'Approved finished Goods Stock' area.

## (iv) Working Space :-

The manufacturing area shall provide adequate space for orderly placement of equipment & material used in any of the operation for which these are employed so as to facilitate easy & safe working & to minimize or to eliminate any risk of mix-up between different drugs, raw materials & to prevent the possibility of cross-contamination of one drug by another drug i.e. manufactured, stored or handled in the same premises.

(i) Health, Clothing, Sanitation & Hygiene of workers :-
All the employees in the factory should be healthy & free from any infectious diseases. Clothing & other apparels of the workers should be clean. They should be dressed in proper uniforms, including cloth or synthetic covering of hands & feet as per the nature of work & the climate.

For personal cleaning, adequate facilities such as clean towels, soap & scrubbing brushes, should be provided. Separate lavatories should be made for men & women and should be located in an area separated from the processing rooms. Facilities such as rooms for changing cloth & to keep personal belonging.

(j) Medical Services :-
The manufacturer shall also provide:
(a) Adequate facilities for first aid.
(b) Medical examination of workers at the time of employment & periodical checkup thereafter by a physician once a year with particular attention being devoted to freedom from infections. Records thereof shall be maintained.

(k) Machinery & Equipments :-
For carrying out manufacturing depending on the size of operation & the nature of product manufactured; suitable equipment either manually operated or operated semi-automatically or full automatic machinery shall be made available. There may include machines for used in the process of manufacture such as crushing, grinding

powdering, boiling, mashing, burning, roasting, filtering, drying, fining, labelling & packing etc.

(l) Batch Manufacturing Records :-
The license shall maintain batch manufacturing records of each batch of ayurvedic, Siddha & Unani drugs manufactured irrespective of the type of product manufactured.
Manufacturing records are required to provide an account of the list of raw materials & their quantities obtained from physical characteristics & chemical tests as may be necessary or indicated in the approved books of Ayurveda, Siddha & Unani mentioned in the First Schedule of Drugs & Cosmetics Act 1940.

(m) Distribution Records :-
Records should be maintained for sale & distribution of each batch of Ayurveda, Siddha, unani drugs. These records facilitate quick & complete recall of the batch whenever needed.

(n) Record of Market Complaints :-
Manufacturers shall maintain a register to record all reports of market complaints received regarding the products sold in the market.

(e) Quality Control :-

Every license is required to provide facility for quality Control Section in his own premises or through government approved testing laboratory.

The quality Control Section shall have the following facilities :

- There should be 150 sq. feet area for quality Control Section.
- References book & samples should be maintained for easy identification of raw drugs.
- Manufacturing record should be maintained for the various processes.
- To verify the finished products, controlled samples of finished products of each batch will be kept till the expiry date of product.
- To supervise & monitor adequacy of condition under which raw materials, semifinished products & finished products are stored.
- Keep record in establishing shelf-life & storage requirements for the drugs.
- Manufacturers who are manufacturing patent proprietary Ayurvedha, Siddha & unani medicines shall provide their own specifications & Control references in respect of such formulated drugs.
- The record of specific method & procedure of prep", i.e. 'Bhavana', 'Mardana' & 'Puta' & the record of every process carried out by the manufacturer shall be maintained
- The standards for identity, purity & strength as given in respective pharmacopoeias of Ayurveda, Siddha, Unani systems of medicines published by government of India shall be complied with.
- All raw materials will be monitored for fungal, bacterial Contamination with a view to minimize such Contamination.

(5) Requirement of Sterile product :

(a) Manufacturing areas :-

For the manufacture of Sterile Ayurvedic, unani & Siddha drugs, separate enclosed areas specifically designed for the purpose shall be provided. These areas shall be provided with air locks for entry & shall be essentially dust free & ventilated with fan air supply. For all areas where aseptic manufacture has to be carried out, air supply shall be filtered through bacteria retaining filters (HEPA filters)

(b) Precaution against Contamination & Misc :-

- The manufacturing operations should be performed in an isolated area of the same building or another building.
- In the process area, an appropriate pressure differential device should be installed.
- An adequate exhaust system should be installed with in the premises.
- Laminar flow Sterile air system should be present for Sterile products.
- All the processes should be carried out as per master formula.
- All the parameters including adequate room temp, relative humidity, volume, filled, leakage & clarity, should be checked & associated results should be recorded.

Part - II

(a) List of Recommended Machinery, Equipment & Minimum Manufacturing Premises required for the manufacture of various Categories of Ayurvedic, Siddha System of Medicine:

1200 Sq. feet Covered area with separate cabins or partitions for each activity. If unani medicines are manufactured in same premises an additional area of 400 sq. feet will be required.

| Sno. | Category of Medicine | Minimum manufacturing space required | Machinery / equipment Recommended |
|---|---|---|---|
| 1. | Anjana/Pisti | 100 Sq. feet | Kharal/mechanized/motorized Kharal, End runner/Ball-mill Sieves / Shifter. |
| 2. | Pills/vati/ Gutika Mattrai & tablets | 100 Sq. feet | Ball-mill, Mass mixer, Granulator drier, tablet Compressing machine, Stainless steel trays, polishing pan in case of Sugar-coated tablets |
| 3. | Kajal | 100 Sq. feet | Earthen lamps for Collection of kajal. Triple Roller mill, End runners, Sieves, S.S. Patila, Filling/packing & manufacturing room should be provided with exhaust fan & ultra violet lamps. |
| 4. | Capsules | 100 Sq. feet | Air Conditioner, De-humidifier, hygrometer, thermometer, capsule filling machine & chemical balance. |

| | | | |
|---|---|---|---|
| 5. | Ointment/Kalkam Pasai | 100 sq. feet | Tube filling machine, crimping machine / ointment mixer, Bird Runner / Mill, SS. storage Castainer, S.S. Patila |
| 6. | Taila / Ghrita Paka | 100 sq. feet | Bhatti, Kadhai / S.S. Patila, S.S. storage Castainers, Filteration equipment, liquid filling machine. |
| 7. | Arishta, Syrup / Kashaya Manufacture | 150 sq. feet | Tincture press, Bhatti Section, Bottle filling machine, filter press / gravity filter, liquid filling machine, P.P. Capping machine. |
| 8. | Churna / Kalka / Manjan / Lepa / Kwatha Churna | 200 sq. feet | Grinder / Disintegrator / Pulveriser / Powder mixer / Sieves / Shifter. |
| 9. | Asava / Arishta | 200 sq. feet. | Fermentation tanks, Containers & distillation plant (where necessary), Filter press, Tincture Press, Bottle washing machine, liquid filling machine |

(b) List of machinery, Equipment & Minimum Manufacturing premises required for the manufacture of various Categories of Unani System of medicine:

1200 square feet Caered area with Separate Cabins, partition for each activity. If Ayurveda / Siddha

medicines are manufactured in same premises an additional area of 400 sq. feet will be required.

| Sno | Category of Medicine | Minimum manufacturing Space required | Machinery / equipment recommended |
|---|---|---|---|
| 1. | Arishal | 100 sq. feet | Grinder / pulveriser, Sieves, S.S. Patilas, Bhatti & other accessories, plant mixer for Khamira |
| 2. | Arq | 100 sq. feet | Distillation plant, S.S. storage tank, Boiling vessel, Gravity filter, Bottle filling machine, Bottle washing machine, Bottle drier. |
| 3. | Habb & tablets | 100 sq feet | Ball mill, Mass mixer, Granulator drier, tablet Compressing machine, Stainless Steel trays, pill making machine. |
| 4. | Surma, kajal | 100 sq. feet | End runner, mixing S.S. vessel. |
| 5. | Marham | 100 sq. feet | Kharal, Bhatti, End runner, Grinder, Pulveriser, Triple roller mill. |
| 6. | Capsule | 100 sq. feet | Pulveriser, Capsule filling machine, Air-conditioner, De-humidifier, Balance with weights, Storage containers, glass. |
| 7. | Sufoof (Powder) | 200 sq. feet | Grinder / pulveriser, Sieves, Trays, Scoops, Powder mixer. |

(c) List of Equipment recommended for in-house quality Control Section :

| (1) Chemistry Section. | (2) Pharmacognosy Section |
|---|---|
| (i) Alcohol Determination Apparatus | (i) Microscope Binocular |
| (ii) volatile oil Determination Apparatus | (ii) Dissecting microscope |
| (iii) Boiling point Determination Apparatus | (iii) Microtome |
| (iv) Melting point Determination Apparatus | (iv) Physical Balance |
| (v) Refractometer. | (v) Aluminium Slide Trays. |
| (vi) Polarimeter. | (vi) Stage Micrometer |
| (vii) viscometer. | (vii) Camera Lucida |
| (viii) Tablet disintegration apparatus. | (viii) Chemicals, Glasswares |
| (ix) Moisture meter. | |
| (x) Muffle Furnace. | |
| (xi) Electronic Balance. | |
| (xii) Magnetic Stirrer. | |
| (xiii) Hot Air oven | |
| (xiv) Refrigerator | |

(xv) Glass/ Steel distillation Apparatus
(xvi) LPG gas Cylinders with Burners
(xvii) water Bath
(xviii) Heating Mantles /Hot Plates
(xix) TLC apparatus with all accessories.
(xx) Paper Chromatography apparatus with accessories.
(xxi) Sieve Size 10 to 120 with Sieve Shaker.
(xxii) Centrifuge Machine.
(xxiii) Dehumidifier
(xxiv) pH Meter
(xxv) limit Test apparatus.