Unit - 4

(A) Evaluation of Drugs

→ **WHO & ICH guidelines for the assessment of herbal drugs** -
Acc. to WHO & ICH guidelines, herbal medicines are defined as " finished, labelled medicinal products that contain active ingredients as aerial or underground parts of plants or other plant materials or combination thereof, whether in the crude state or as plant prep ".

WHO guidelines for assessment of herbal Drugs:

Objectives -

- Guiding principle for evaluating the quality w.r.t the safety of herbal medicines with specific reference to Contaminants & residues.
- Model criteria for using while identifying possible Contaminants & residues.
- Example of methods & techniques.
- Example of practical procedures for controlling the quality of finished herbal products.

Assessment of Quality, Safety, & Intended use - (Efficacy)

WHO has given the guidelines which for quality check of herbal drugs by checking the quality, safety, efficacy & intended use of herbal drugs. Acc. to WHO after qualifying these parameters, the herbal drugs can be ready to market for sale.

Assessment of Quality :-

→ Crude Plant Material :-

- The botanical definition including genus, species, authority should be given to ensure correct plant identification.
- Definition & description of the plant part from which the medicine is derived (eg- leaf, flower, root) should be provided, along with an indication of whether fresh, dried or traditionally processed material is used.
- The active & characteristic constituents should be specified & content limits should be provided.
- Foreign matter, impurities & microbial content should be defined or limited.
- Voucher specimen, representing each batch of plant material processed, should be authenticated by a qualified botanist & stored for 10 years. A batch no. should be assigned & put on the product label.

→ Plant prep^{n} :-

Plant prep^{n} should include powdered plant materials, extract, tinctures, fatty or essential oils, expressed juices & prep^{n} whose production involves a fractionation, purification or concentration process. The manufacturing process should be described in detail. If any other substance is added during the manufacture, to adjust the plant prep^{n} to a certain level of active or characteristic constituents or for any other purpose, the added substance

should be mentioned in the procedure description.
A method for identification & assay of the plant prep" should be added. If the identification of an active principle is not possible, it should be sufficient to identify a characteristic substance or mixture of substances (eg. chromatographic fingerprint) to ensure consistent quality of prep".

→ Finished products :-
The manufacturing procedure & formula including the amount of excipient should be described in detail. A method of identification & quantification of the plant material in the finished product should be defined. If an active principle cannot be identified, it should be sufficient to identify a characteristic substance or mixture of substance (eg. chromatographic fingerprinting) to ensure consistent quality of the product.
For imported finished products, confirmation of regulatory status in the country of the origin should be required. The WHO certificate scheme on the quality of the pharmaceutical products moving in International Commerce should be applied.

→ Stability :-
The physical & chemical stability of the product in the final marketing container should be tested under defined storage conditions & the shelf-life should be established.

Assessment of Safety :

The part should cover all the relevant aspects of the safety assessment of a medicinal product. Has been traditionally used without demonstrated harm, no specific restrictive regulatory action should be undertaken unless new evidence demands a revised risk benefit assessment.

Toxicological Studies :-

If any toxicological studies are available, they should be part of the assessment. If a toxicological risk is known, toxicity data have to be submitted. Risk assessment, whether it is independent of dose (eg - Special danger allergies) or whether it is a function of dose should be documented.

Assessment of Efficacy :

This part should cover all the important aspects of efficacy assessment. A review of the relevant literature should be carried out & copies provided of the original articles or proper references to them.

Activity :-

The pharmacological & clinical effects of the active ingredients & their constituents with therapeutic activity should be described.

Evidence required to support indication :-

The indication for the use of medicine should be specified. In case of traditional medicines,

the requirements for proof of efficacy shall depend on the kind of indication.

Intended use:

Product Information for the Consumer :-

The labeling of the products & the package insert should be understandable to the consumer/patient. The package information should cover all necessary information on the proper use of product:

(1) Product name
(2) Quantitative list of active ingredients.
(3) Dosage form.
(4) Indication :
   (a) Dosage (specified for children & elderly)
   (b) Administration mode
   (c) Duration of use
   (d) major adverse effects.
   (e) overdosage information.
   (f) Contraindication, warning, precaution, & major drug indication
   (g) use during pregnancy & lactation.
(5) Expiry date
(6) Lot no.
(7) Holder of the marketing authorization.

ICH Guidelines for assessment of herbal drugs :

ICH (International Conference on harmonization) is an international organization, it developed the guidelines regarding assessment or quality check of herbal drugs.

Objectives -

- Make economical use of human, animal & material resources.
- Elimination of unnecessary delay in the global development & availability of new medicines.
- Maintaining safeguards on Quality, Safety, efficacy & regulatory obligation to protect public health.

ICH Guidelines for assessment of herbal drugs -
ICH guidelines deal with four criteria (QSEM) in assessment of herbal drugs.

(1) Quality (Q) :-
Those relating to chemical & pharmaceutical Quality assurance (Stability testing, Impurity testing)

(2) Safety (S) :-
Those relating to in-vitro & in-vivo preclinical studies (Carcinogenecity Testing, Genotoxicity testing).

(3) Efficacy (E) :-
Those relating to clinical studies in human subject. (Dose response studies, Good clinical practices).

(4) Multidisciplinary (M) :- which
Cross-cutting topics do not fit uniquely into one of the above categories (Med DRA, ESTRI, M3, CTD, M5)

Overview of ICH -

Quality Guidelines -

Q1 : Stability (Q1A - Q1F)
Q1A - Stability testing of new substances & products.
Q1B - Photostability testing of new drug substance & product.
Q1C - Stability testing for new dosage forms.
Q1D - Bracketing & matrixing designs of stability testing of new drug substances & products.
Q1E - Evaluation of stability data.
Q1F - Stability data package for registration application in climatic zone III & IV.

Q2 : Analytical validation

Q3 : Impurities (Q3A - Q3D)
Q3A - Impurities in new drug substance.
Q3B - Impurities in new drug products.
Q3C - Impurities - guidelines for residual solvents.
Q3D - Impurities - guidelines for elemental impurities.

Q4 : Pharmacopeias (Q4A - Q4B)
Q4A - Pharmacopeial harmonisation
Q4B - Evaluation & recommendation of pharmacopeial texts for use in the ICH regions.

Q5 : Quality of Biotechnological products (Q5A - Q5E)
Q5A - viral safety evaluation
Q5B - Genetic stability
Q5C - Stability of biotechnological products.
Q5D - Cell substrates
Q5E - Comparability of biotechnological products.

Q6 : Specification (Q6A - Q6B)
Q6A - Test procedures & acceptance criteria for new drug substances & new drug products - Chemical substances
Q6B - Test procedures & acceptance criteria for biotechnological products.

Q7 : GMP for active pharmaceutical ingredients.

Q8 : Pharmaceutical development.

Q9 : Quality risk management.

Q10 : Pharmaceutical quality system.

Stability guidelines -

S1 : Carcinogenicity studies (S1A - S1C)
S1A - Need for carcinogenicity studies of pharmaceutical.
S1B - Testing for carcinogenicity of pharmaceuticals.
S1C - Dose selection for carcinogenicity studies of pharmaceuticals.

S2 : (Genotoxicity studies): Guidance on genotoxicity testing & data interpretation for pharmaceuticals intended for human use.

S3 : Toxicokinetics & Pharmacokinetics (S3A - S3B)
S3A - Note for guidance on toxicokinetics : Assessment of systemic exposure in toxicity studies.
S3B - Pharmacokinetics : Guidance for repeated dose tissue distribution studies.

S4 : (Toxicity testing) : Duration of chronic testing in animals (rodent & non-rodent toxicity testing)

S5 : (Reproductive testing) : Detection of toxicity to reproduction for medicinal products & toxicity to male fertility.

S6 : (Biotechnological products) : Preclinical safety evaluation of biotechnology derived pharmaceuticals

S7 : Pharmacology studies. (S7A - S7B)
S7A - Safety pharmacology studies for human pharmaceuticals
S7B - Non-clinical evaluation of the potential for delayed ventricular repolarisation by human pharmaceutical.

S8 : (Immunological studies) : Immunotoxicity studies for pharmaceuticals.

S9 : Non-clinical evaluation for anticancer pharmaceuticals.

S10 : Photosafety evaluation of pharmaceuticals.

Efficacy Guidelines

E1: Clinical safety for drugs used in long term treatment.

E2: Pharmacovigilance (E2A - E2F)

E2A - Clinical safety data management.

E2B - Clinical safety data management data elements for Transmission of individual case Safety report.

E2C - Clinical safety data management: periodic Safety update reports for marketed drugs.

E2D - Post approval safety data management: definition & Standards for expedited reporting.

E2E - Pharmacovigilance planning.

E2F - Development safety update report.

E3: Clinical study reports.

E4: Dose response studies.

E5: Ethnic factors

E6: Good clinical practice

E7: Clinical trials in geriatric population

E8: General Consideration for clinical trials

E9: Statistical principles for clinical trials.

E10: Choice of Control group in clinical trials.

E11 : Clinical trials in paediatric population.
E12 : Clinical evaluation by therapeutic category.
E14 : Clinical evaluation.
E15 : Definitions in pharmacogenetics / pharmacogenomics
E16 : Qualification of genomic biomarkers.
E17 : Multi-regional clinical trials.
E18 : Genomic sampling methodologies.

Multidisciplinary Guidelines -

M1 : MedDRA (Medical dictionary for regulatory activities) terminology.
M2 : ESTRI (Electronic Standards for the Transfer of Regulatory information).
M3 : Non-clinical Safety studies.
M4 : Common technical document. (CTD)
M5 : Data elements & Standards for drug dictionaries.
M6 : Gene therapy
M7 : Genotoxic impurities.
M8 : electronic Common Technical Document (eCTD) studies

→ Stability of Herbal drugs -

" Sasirujata avadhi" (shelf-life) denotes the time period during which the virya (potency) of any drugs remains unaffected & above certain threshold beyond which it may lose its potency to some extent but not completely devoid of it provided that it is stored in the mentioned condition.

Stability is the capability of a specific formulation in a particular container / closure system to remain within its physical, chemical, toxicological microbiological, therapeutic specification & is always

expressed in terms of shelf-life.

Types of Stability testing Methods:

(1) **Accelerated testing** - The product is subjected to a several high temperatures, humidity, light intensity, etc that accelerates degradation & the amount of heat required to degrade the product is determined so as to predict the shelf-life.

The concept is based upon Arrhenius eqn that describes the relationship b/w storage temp. & deterioration rate.

$$\log \frac{K_2}{K_1} = -Ea / 2.303R \left(1/T_2 - 1/T_1\right)$$

Where,

K_1 & K_2 = rate constant at respective temp. T_1 & T_2

Ea = activation energy

R = gas constant

Accelerated stability studies are usually used for product with longer shelf-life.

(2) **Real time (long-term) testing** -

It is normally performed for longer duration to allow significant degradation of the product under specified storage conditions.

(3) **Intermediate testing** -

These are mainly conducted when the accelerated studies for general case failed to meet the

acceptance criteria & are designed to moderately increase the rate of degradation for a drug intended to be stored long-term at 25°C.

(4) Stress testing :-
It includes the effect of temperature, humidity (≥ 75% RH) oxidation, photolysis, hydrolysis.

(5) Forced Degradation testing :-
It is performed with objective to provide intrinsic stability assessment of the drug, to elucidate the possible degradation pathway by identifying the likely degradation product & to have an idea of the stability of the analytical process applied for the drug.

Climatic Zones for Stability testing :
For stability testing purpose, the whole world has been divided into four zones as per environmental condition & is derived on the basis of mean annual temperature & relative humidity.

Climatic zone	Climate	Countries	Long term condition
I	Temperate	UK, Northern Europe, US	21°C / 45% RH
II	Subtropical & Mediterranean	Japan, Southern Europe.	25°C / 60% RH
III	Hot & Dry	Iraq, India	30°C / 35% RH
IVa	Hot & humid	Iran, Egypt	30°C / 65% RH
IVb	Hot & very humid	Brazil, Singapore	30°C / 75% RH

Stability Protocol :

Stability protocol should include information on the following :

(i) Batches tested.
(ii) Unit Composition
(iii) Container- closure System
(iv) Literature & supporting data
(v) Stability specifications.
(vi) Analytical methods i.e. Stability indicating.
(vii) Stability plan.
(viii) Tabulated test results.
(ix) Analysis of data.
(x) Shelf- life proposal
(xi) Post- approval commitments.

Stability testing storage conditions for drugs as per ICH & WHO -

Intended Storage Condition	Stability test method	Test temp. & humidity (periods in months) ICH	Test temp. & humidity (periods in months) WHO
Room temp.	long term	25 ± 2°C/60 ± 5% RH (12)	25 ± 2°C/60 ± 5% RH or 30 ± 2°C/65 ± 5% RH (12)
	Intermediate	30 ± 2°C/65 ± 5% RH (6)	30 ± 2°C/65 ± 5% RH (6)
	Accelerated	40 ± 2°C/75 ± 5% RH (6)	40 ± 2°C/75 ± 5% RH (6)
Refrigerated	long term	5°C/ambient (12)	5 ± 3°C
	Accelerated	25 ± 2°C/60 ± 5% RH (6)	25 ± 2°C/60 ± 5% RH or 30 ± 2°C/65 ± 5% RH
Freezer	long term	-20°C/ambient (12)	-20°C ± 5%

Part-B
Patenting & Regulatory Requirements of Natural Products

→ Definition of the terms :-

:: Patent -
A patent is an exclusive right granted for an invention that provides a new way of doing something, or that offers a new technical solⁿ to a problm.
A patent provides patent owners with protection for their inventions. Protection is granted for a limited period, generally 20 years.
Patents provide incentives to individuals by recognizing their creativity & offering the possibility of material reward for their marketable inventions.
These incentives encourage innovation, which in turn enhances the quality of human life.

Kinds of Inventions that can be protected by Patent :-
An invention must, in general, fulfil the following conditions to be protected by a patent :-

- It must be of practical use.
- It must show an element of 'novelty' meaning some new characteristic that it is not part of the body of existing knowledge in its particular technical field. That body of existing knowledge is called 'prior art'.
- The invention must show an 'inventive step' that could not be deduced by a person with average knowledge of the technical field.
- Its subject matter must be accepted as 'patentable' under law.

In many countries, scientific theories, mathematical methods of medical treatment are not generally patentable.

Process to Grant Patent :-
Patent are granted by national patent offices or by regional offices that carry out examination work for a group of countries (eg: Indian Patent office (IPO), The European patent office (EPO), The American Intellectual Property organization (OAIP)). Under such regional systems, an applicant request protection for an invention in one or more countries & each country decides whether to offer patent protection within its borders.
The WIPO (World Intellectual Property organization) provides for the filing of a single international patent application that has the same effect as national application filed in the designated countries.

Intellectual Property Rights (IPR) :-

Intellectual Property :-
Intellectual property refers to creation of the mind: invention, literary and artistic works, symbols, names & images used in commerce.
Intellectual property is divided into 2 categories:
(i) Industrial property:
It includes patent for invention, trademarks, industrial design & Geographical indications

(iii) Copyright:
It covers literary works (such as novels, poems & plays) films, music, artistic works (eg- drawing, painting, photographs & sculptures) & architectural design.

Intellectual Property Rights :-

Definition -
IPR are like any other property rights. They allow creators, or owners of patents, trademarks or copyrighted works to benefit from their own work or investment in a creation.

These rights are outlined in Article 27 of the universal declaration of Human rights, which provides for the right to benefit from the protection of moral & material interests resulting from authorship of scientific, literary or artistic production.

The importance of intellectual property was first recognized in the Paris Convention for the Protection of Industrial property (1883) and the Berne Convention for the Protection of literary & Artistic works (1886).

Both treaties are administered by the WIPO.

Importance of IPR -

(i) By action of IPR the progress & well-being of humanity rest on its capacity to create & invent new works in the areas of technology & culture.
(ii) The legal protection of new creations encourages the commitment of additional resources for further innovation.
(iii) The promotion & protection of intellectual property spurs economic growth, creates new jobs & industri

& enhances the quality & enjoyment of life.

(iv) An efficient & equitable intellectual property system can help all countries to realize intellectual property's potential as a catalyst for economic development & social & cultural well-being.

(v) The intellectual property system helps strike a balance between the interests of innovators & the public interest, providing an environment in which creativity & invention can flourish, for the benefit of all.

Farmer's Right –

Introduction :-

The Protection of Plant varieties & Farmers Rights' Act (PPVFR act) seeks to address the rights of plant breeders & farmers on an equal footing. It affirms the necessity of recognizing & protecting the rights of farmers w.r.t the contributions they make in conserving, improving & making PGR (Plant Growth Regulator) available for the development of new plant varities. Under the Act, PBR's (Plant breeder's right) allow breeders to hold exclusive rights to produce, sell, market, distribute, import or export the propagating material of a registered variety.

Definition of Farmer's right :-

The PPVFR Act recognizes the multiple roles played by farmers in cultivating, conserving,

developing & selecting varities. With regard to developing or selecting varieties, the Act refers to the value added by farmers to wild species or traditional varieties through selection & identification of their useful traits.
Accordingly, farmer's right encompass the roles of farmers as users, conservers & breeders.

Nine Specific Rights of Farmers :-

Right 1 - Access to Seed -
The act provides the farmers the right to save, use, exchange or sell seed. But, the farmers cannot sell the seeds in a packed form labelled with registered name.

Right 2 - Benefit - Sharing -
All Indian legal entities who provide PVP to breeder for developing new varieties, including farmers shall receive a fair share of the benefits from the commercial gains of the registered varieties.

Right 3 - Compensation -
The breeder should provide information about the expected performance of registered variety. If the materials fails to perform as expected, the farmers may claim for compensation under the act.

Right 4 - Reasonable Seed price -
Farmers have the rights to access seed of registered varities at a reasonable price. When this condition is not met, the breeder's exclusive right over the variety is suspended under the provision concerning

Compulsory licensing, & the breeder is obligated to license the seed production, distribution & sales of the variety to a competent legal entity.

Right 5 - Farmer's Recognition & Rewards for Contributing to Conservation -

The Act provides for establishment of National Gene Fund through the work of farmers are recognized & rewarded.

Right 6 - Registration of Farmer's varities -

The Indian PPVFR Act allows for the registration of existing farmer's varieties that fullfill requirement for distinctness, uniformity, Stability & denomination but doesn't include that of novelty. This right provides farmers with a one-off opportunity for a limited period of time, from the moment when a crop species is included in the crop portfolio under the PPVFR Act for the registration.

Right 7 - Prior Authorizations for the Commercialization of essentially derived varities -

When farmer's varieties whether extant or new are used by a third party as source material for the development of an essentially derived variety, the farmers need to provide prior authorization for its commercialization. Such a process can allow farmers to negotiate the terms of authorization with the breeder, which may include royalties, one-off payments, benefit-sharing, etc.

Right 8 - Exemption from registration fees for farmers -
Under the PPVFR Act, farmers have the privilege of being completely exempt from paying any kind of fees or other payments that are normally payable for variety registration, test for distinctness, uniformity & stability (DUS) & other services rendered by the PPVFR Authority, as well as for legal proceedings related to infringement or other causes.

Right 9 - Farmers protection from accidental infringement
If a farmer can somehow prove before court that he or she was not aware of the existence of any rights at the time of an infringement on any such rights, as detailed in the PPVFR Act, he or she will not be charged.

3. **Plant breeder's right -**
Plant Breeder's right (PBR) also known as plant variety rights (PVR) are rights granted to the breeder of a new variety of plant that give the breeder exclusive control over the propagating material (seed, cutting, division, tissue culture) & harvested material (cut flower, foliage) of a new variety for a no. of years.

With these rights, the breeder can choose to become the exclusive marketer of the variety or to license the variety to others.

Characters of plant variety to come under plant breeder's right :-

In order to qualify for these exclusive rights, a variety must be new, distinct, uniform & stable.

New - If it has not been commercialized for more than one year in the country of protection.

Distinct - If it differs from all other known varities by one or more important botanical characteristics such as height, maturity, colour, etc.

Uniform - If the plant characteristics are consistent from plant to plant with in the variety.

Stable - If the plant characteristics are genetically fixed & therefore remain the same from generation to generation or after a cycle of reproduction in the case of hybrid varieties.

The breeder must also give the variety an acceptable "denomination", which becomes its generic name & must be used by anyone who markets the variety.

Process to grant Plant variety Rights :-

Typically, plant variety rights are granted by national offices, after examination. Seed is submitted to the plant variety office, which grow it for one or more seasons, to check that it is distinct, Stable & uniform. If these tests are passed, exclusive rights are granted for a specified period (typically 20/25 years or 25/30 years

for trees & vines). Annual renewal fees are required to maintain the rights.

∵ **Bioprospecting =**

Bioprospecting is the search for & commercialization of new products derived from nature.

Bioprospecting refers to the search for valuable active chemical compounds in nature & accessing natural resources through legal means, securing prior informed consent from the custodians of the relevant natural resources & promoting equitable benefit sharing agreements with appropriate parties.

Process of Bioprospecting :-

As a process, it generally consist of 4 phases :

Phase 1 - On-site collection of samples.

Phase-2 Isolation, characterisation & culture of specific compounds.

Phase-3 - Screening for potential uses, such as pharmaceuti

Phase-4 Product development & commercialization including patenting, trials, sales & marketing.

legislation & Regulation :-

legislation & regulation should -

(i) Ensure that clear conditions & procedures govern access to genetic resources.

(ii) Make access subject to written agreement based on prior informed consent.

(iii) Require fair & equitable sharing of the benefits.

Biopiracy :-

Definition :-

The unethical or unlawful appropriation or commercial exploitation of biological materials that are native to a particular country or territory without providing fair financial compensation to the people or government of that country or territory.

Or

Biopiracy is the practice of commercially exploiting naturally occurring genetic material or biochemical. Most of the indigenous people possess a traditional knowledge that mainly comprises of genetic diversity & biological feature of the natural environment from generation to generation.

Some of the traditional knowledge that is relevant to global survival includes the following components :

(i) Medicinal plants.
(ii) Farming or agriculture.
(iii) Varieties of food crops.

The essential components for the survival of rural & indigenous people include conservation of habitat, species & biodiversity.

Examples of Biopiracy :-

(i) Biopiracy of African Super-Sweet berries :
Pentadiplandra brazzeii is a plant found in the west of South Africa. It is a vital

source of protein known as Brazzein. Here, people use as a low-calorie sweetner. It is known to be 2,000 times sweeter than sugar.

Recent developments include isolation of the gene encoding brazzein that has been sequenced & patented in the USA.

(2) Patenting of Azadirachta indica - Neem :

Since ancient times, neem has proved to be useful in several ways. Indians have shared their knowledge regarding neem across the globe. In the year 1994, U.S. department of Agriculture & an American company - W.R. Grace received a European patent that include various methods that are used for controlling fungal infections in plants by using a composition extracted from neem.

(3) Biopiracy of the Enola bean :

It was named after the wife of Larry Proctor, who patented it in 1999. Enola bean is a variety of Mexican yellow bean. Farmers in the North Mexico depended on sales of this bean. The patent-holder subsequently used as a large no. of importers of Mexican yellow beans. As a result, it caused an economic damage to farmers. A lawsuit was filed by farmers & the result was in favour of farmers as ruled by U.S. Patent & Trademark office.

→ Patenting Aspects of Traditional Knowledge & Natural products. Case Study of Curcuma & Neem:

Definition :-
Traditional knowledge is the long standing tradition & practices of indigenous peoples & communities. These tradition & practices passed on from generation to generation can include different aspects of a particular culture including the arts & farming techniques.

Protection of Traditional knowledge :-
Two types of intellectual property protection are:

(1) Defensive Protection -
It aims to stop outside the community from acquiring intellectual property right over traditional knowledge. Defensive strategies can be used to protect sacred cultural manifestation such as sacred symbols or words for being registered as trademark.

(2) Positive Protection -
It aims to grant rights permitting the communities to promote their traditional knowledge, control its uses, benefit from its commercial exploitation.

Patenting Requirement in Traditional Knowledge :-

- As per the guidelines the claimant is required to declare the 'geographical origin' of the biological material used in form 1.
- The permission from the National Biodiversity Authority is essential for use of any biological material in India.
- Patents may be granted for 'unique' combination, like those involving the selection of specific ingredients, in specific proportion, processed under specific condition. These unique formulation may be aimed at displaying better synergy or antagonistic activity, better stability & better absorption.
- The guidelines refuse any claims for patents pertaining to the extracts / alkaloids of the plant already mentioned in the TKDL as 'Prior art'.

Traditional Knowledge Digital library (TKDL) :-

TKDL is a unique database & a form of proprietary database which integrates many diverse knowledge systems in diverse knowledges.

This was created on the base of 148 books in India that was based on the olden day system of medicine & this includes other Prior Art books in India.

The patent examiners are those who have signed TKDL Access Agreement & these knowledge & information are available only to them.

Case Study of Curcuma :

Introduction :

Turmeric is a tropical herb grown in East India. Turmeric powder is widely used in India as a medicine for treating common cold, as a blood purifier, an antiparasitic for many skin infection, an essential food ingredient in cooking & a dye.

Patent Case Study of Turmeric –

(a) Patent Issue :

In 1995, US Patent was awarded to Medical Centre of University of Mississippi for the use of wound healing property.

(b) India's Claim :

Dr R.A. Mashelkar who was the Director of Council of Scientific & Industrial Research (CISR) during period of 1995 to 2006 opposed the patent granted to the Medical Centre of Mississippi University & worked hard for awakening India's traditional Knowledge of Turmeric.

(c) Arguments by Indian Scientists :

The claim was supported by documentary evidence which was an old newspaper dated 1953 printed & published by Indian Medical Association, & there work also evidence produced which includes old & ancient texts in Sanskrit.

(d) Judgement :
In 1998 April, the judgement favoured CSIR which was based on the argument that was praed with sitting documentary evidence that Turmeric was being in use by Indian people since ancient period of time.

Case Study of Neem :

Introduction :-
The Neem tree is a native evergreen species of tropical countries like India & other such Southeastern countries. Neem is called as 'the village Pharmacy' in India for its healing property & it is used in medicine & mostly in Ayurveda from its very beginning.
The Neem is called as 'Arista' which is a Sanskrit word which means imperishable or Complete It is used as an antiinflammatory, antipyretic, antiseptic, antifungal, antiviral medicines.

Patent Case Study of Neem -

(a) Biopiracy :
The term biopiracy means the theft of Several genetic resources & materials mainly the plant materials in the form of obtaining patent! Once a material is patented, the owner could possibly prevent that thing form being accessed by any other person even though the one is real owner of that property. Thus, by patenting the traditional knowledge of indigenous people the Corporate can restrict the people from use of their own traditional knowledge & thus it affects the livelihood of native people.

(b) Problem raised in Neem Patent :

In 1971, a timber importer from US imported neem seeds to plant neem trees in his headquaters in Wisconsin. He also conducted performance & safety tests upon the pesticidal properties of neem & got clearance from the US Environment Protection agency k/n as EPA. After 3 years he sold the patent to a multinational corporate company which is k/n as W.R. Grace & Co. & By the year 1985, Several US & Japanese corporation were trying to find & formulation of emulsion for toothpaste production it of neem. Subsequently in 1992, the corporate WR Grace & Co. claimed rights for the emulsion be gotten out of neem seeds. And by this it began to sue Indian companies for making such emulsions.

(c) Dispute :

Acc. to Indian's claim, it was stated that neem is an indigenous product & it is still in practice as a form of traditional knowledge in India. It was also said that Neem if granted patent it would affect the poor farmers & by this the Indian economy will also be harmed.

(d) Neem campaign in India :

A group of individuals & several NGO's initiated their neem campaign & this was done to mobilise the worldwide people for support & to protect the traditional knowledge systems & also protect Indian traditional products from biopiracy. The neem case was the first initiative

to challenge US & European patents with regard to biopiracy.

(6) Case Judgement:

On July 30, 1997, the European Patent office (EPO) accepted the arguments of Indian scientists thus this resulted in rejection of patent granted by the US patent office to WR Grace & Co. The argument which was accepted on whole was the use of neem & its products in India for a period of more than 4000 years.

Part - C
Regulatory Issues

→ **Herbal Drug regulation in India** :- Important Provisions relating to the manufacture & Control of 'Ayurvedic, Siddha, Unani' (ASU) drugs have been prescribed in the drugs & Cosmetic act. This act describes the formation of 'drugs technical advisory board' (DTAB) which consists of various nominated members & 'drugs Consultive committees' (DCC).

:) **ASU - DTAB** -
The Central government shall Constitute a board by notifying in the official gazette. The board shall advice the Central as well as state governments on technical matters arising out of the Section 33-C of the drugs & Cosmetic & Carry other functions assigned.

(a) **Constitution of the board** :
The board shall Consist of the following members :

(i) **Ex - Officio Members** -
(1) The Director General of Health service.
(2) The Drugs Controller, India.
(3) Director of the Central Drugs laboratory, Calcutta.

(ii) **Members nominated by the Central Government** -
(1) A government analyst.
(2) A pharmacognosist.
(3) A phytochemist.
(4) Two persons from the members of the Ayurvedic

Pharmacopoeia committee, one from the members of the Unani Pharmacopoeia committee, & one from the members of the Siddha Pharmacopoeia committee.

(5) A teacher in Dravyaguna & Bhaishjya Kalpana.
(6) A teacher in Ilmul-Adwia & Takhis-wa-Dawasazi.
(7) A teacher in Gunapadam.
(8) Three persons, one each to represent the Ayurvedic, Siddha & Unani drug industry.
(9) Three persons one each from the practitioners of Ayurvedic, Siddha, Unani & Tibb system of medicine.

(b) Functioning of the Board:

A chairman, a secretary & other clerical staff are appointed by the Central government. Nominated members hold office for 3 years & can be re-nominated.

ASU-DCC

The Central government may constitute an advisory committee as mentioned in the section 33-D of the Drugs & Cosmetics Act. This committee may advice the Central & State governments & the ASU-DTAB on any matter for the purpose of securing uniformity in the administration of this act throughout India.

Constitution & Functioning of DCC:

- The ASU-DCC shall consist of two persons nominated by the Central government & one person from the state government who act as a representative of the respective government.
- The ASU-DCC shall meet when required to do so by the Central government & shall regulate its own activit

as per their requirements.

→ Regulation for the manufacture of ASU drugs - Schedule L of drugs & Cosmetic Act:

The Sections 33-EEB of the drugs & Cosmetics act describes the regulations for the manufacture & the sale of ASU drugs. The act has set some standards related to the hygienic condition, factory premises, prohibition of manufacture & sale of certain drugs & penalties for contravention of this act.

The following requirements are taken into account:

(A) Requirement of factory premises & hygienic condition- As per the act, it is mandatory to maintain proper hygienic condition in the factory premises along with the following requirements:

- Factory or industry involved in the manufacture of ASU drugs should not be situated adjacent to open sewage, drainage, tannery or any other factory which produces obnoxious odour, large quantities of waste, dust or smoke.
- The premises of manufacturing unit should be clean, hygienic & free from insects, rodents, & other contaminations.
- The walls & floors of manufacturing rooms should be smooth, easily cleanable with water & should not accumulate dust or waste products.
- The water is used in the manufacture should be pure & drinking quality. It should be free from pathogenic organisms. Adequate facility should be.

provided to process the containers and closures for washing, cleaning, drying, etc & it should be separated from the manufacturing unit.

- Suitable agreements shall be provided for disposing waste water & other materials in a manner that it does not affect the health of people in the surrounding areas.
- Personnel working in the factory should be free from contagious diseases.
- Appropriate dress should be provided to the workers based on the nature of their work.
- Adequate facilities for personal cleanliness such as soap, towel, antiseptics should be provided.
- Facilities of drinking water & separate washrooms should be provided for men & women.

(B) Prohibition of manufacture & sale of certain ASU drugs

The act prescribes some criteria to prohibit the manufacture & sale of certain ASU drugs which are not manufactured or sold in accordance of the rules.

The following categories of ASU drugs can be prohibited from manufacture & sale:

- Any misbranded, adulterated or spurious ASU drugs.
- Any proprietary or patented medicine which does not display the list of all ingredients on the label of the containers.
- The selling, stocking & distribution of any ASU drugs which has been manufactured in contravention of the provision of this Act.
- The manufacture, sale & distribution of any ASU drugs for which license has not been issued by the prescribed authority.

- The above rules donot apply to vaidyas & hakims who prepared ASU drugs for the use of their own patients.
- The above rules donot apply to ASU drugs which are manufactured in small quantities for the purpose of examination, test or analysis.

(C) Power of Central government to prohibit the manufacture sale & distribution of ASU drugs in public interest -

The Section 33-EED of the drugs & Cosmetics act prescribes certain power of the Central government based on which the government can prohibit the manufacture, sale & distribution of ASU drugs which involve any risk to humans or animals or such drug doesnot have therapeutic value as claimed by the manufacturer or any misbranded & spurious drugs.

Hence, in such circumstance the govt. may prohibit the manufacture, sale & distributin of drugs in public interest.

(6)

(D) Penalty for the manufacture, sale & distribution of prohibited ASU drugs -

As prescribed under the section 33-1 of the drugs & Cosmetics act, any person himself or his behalf is engaged in the manufacture, Sale & distribution of prohibited ASU drugs, penalty has been fixed as per the following guidelines:

- Any ASU drugs which is deemed to be adulterated or manufactured without a valid license shall be punishable up to one year imprisonment & with fine upto ₹2000.
- Any ASU drugs which is deemed to be spurious shall be punishable with imprisonment upto 1 year to 3 years & with fine upto ₹ 5000.
- Any ASU drugs which contravenes any other provision of the act shall be punishable with imprisonment upto 3 months & with fine upto ₹ 500.

(6) Manufacture on more than one set of premises -
ASU drugs are manufactured on more than one set of premises, a separate application shall be made & a separate license shall be obtained for each premises.