REFERENCE ID: STSH180249

TITLE: COMPARISON OF SIMILARITIES AND DISSIMILARITIES BETWEEN 20 PLANT BASED MEDICINES IN AVAILABLE PHARMACOPOEIAS.

1.INTRODUCTION:

Pharmacopoeia is an official compendium of a country related to regulatory standards of drugs manufactured and practiced in the political zone of that country. Pharmacopoeia, derivative of the Greek word "pharmakopoiia" meaning "drug making or to make a drug"^[1]. The pharmacopoeia contains quality specification of medicines which demonstrates the intensity, strength & purity of medicine. The text has a detail encryption of pharmaceutical starting materials, excipients, intermediates and finished pharmaceutical products ^[2]. It is a book of standards applicable to drug substance and their dosage forms of common usage in a country. It is prepared by recognized authority appointed by the Government of a particular country ^[2].

The World's first accepted pharmacopeia was the "Dispensatorium of Valerius Cordus" in the year 1546, later it was called as "Nuremberg Pharmacopoeia . In addition to Homoeopathic Pharmacopoeia, many systems of medicine such as Ayurveda [3], Unani [4], Siddha [5], Chinese traditional Medicine [6] has similar pharmacopoeias. Recently the Pharmacopoeias are enclosing the DNA barcoding and quantitative metabolomics that are important in ascertaining potency, purity, consistency, safety of pharmacopoeial drugs [1,11]. The study helps in qualifying data in country to country variation in regulating requirements for homeopathic medicine manufacturing and practice. The current pharmacopoeia structure in various countries are the approach of harmonization attempts for unknown application of standards.

In spite of many differences in the regulation of medicines among countries, certain principles are to be considered to regulate the quality of medicines. The drug must possess some properties for the regulation and in providing the therapeutic value ^[7].

2.REVIEW OF LITERATURE:

2.1. HOMOEOPATHIC PHARMACOPOEIA:

First Homoeopathic Pharmacopoeia is published by Carl W Caspari of Leipzig, Germany in 1825 named "Homoeopathic and Dispensatorium Fur Artze and Apotheker". Second Homoeopathic pharmacopoeia was British Homoeopathic Pharmacopoeia which is published in the year 1870 in London. It was published further in two editions in 1876 & 1882. Third Pharmacopoeia was published in 1897 by American Institute of Homoeopathy named "Homoeopathic pharmacopoeia of United States". It was revised and published in 1901 as second edition. Then Homoeopathic Pharmacopoeia Francaise was published in 1898. Brazillian Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia named "Farmacopoeia Homoeopathic Pharmacopoeia homoeopathic Pharmacopoeia".

The Homoeopathic Pharmacopoeia of Different Countries include India , German , American, British , France, Mexico , Brazil ,etc. The monographs available for herbal homoeopathic preparations were France (320), Germany (120), Mexico (558) [2], India (567) [12]. Homoeopathic pharmacopoeia of India had been developed in 1962 on the lines of American, German and British Homoeopathic Pharmacopoeia with the objective of preparation of pharmacopoeia of therapeutically useful proven Homoeopathic Drugs. Homoeopathic pharmacopoeia of India had been published in totally 9 volumes and 919 homoeopathic drugs of various origin [7].

2.2. PHARMACOPOEIA - MONOGRAPHS:

Description of each drugs or preparations included in a Pharmacopoeia are called Monographs. The monographs should be in particular format to define the uniformity of Pharmacopoeia. It may be Botanical, Zoological, Chemical, Metal, Microbiological, etc ^[7]. The Botanical/Zoological monographs of Homoeopathic pharmacopoeia of India explored,

- Botanical name,
- Family,
- Synonym,
- Common Name,

- Description,
- Distribution,
- Parts used
- Macroscopical,
- Microscopical,
- History and Authority,
- Preparation methods and Cautions ^[7,12].

The Chemical / Metal monographs contains

- Pharmacopoeial title with abbreviation,
- Chemical formula with molecular weight,
- Common names,
- Detailed Descriptions such as solubility details,
- Melting point,
- Specific gravity,
- Loss of drying, sulphated ash, etc.,
- Identification, Assay of chemicals,
- History and Authority,
- Preparation,
- Cautions.

The Microbiological Monographs explain the

- Pharmacopoeial title with abbreviation,
- Microbiological name of drugs,
- History and Authority,
- Biological distribution of bacteria or virus,
- Source of preparation of homoeopathic drug,
- Morphology of organism,
- Cultural characteristic feature of organism,
- Biological reaction of organism,
- Preparation,
- Storage details of drug,
- Cautions ^[7].

World Health Organisation suggested the pattern for monographs in medical plants ^[26], i.e.,

- Definition.
- Synonyms.
- Description.
- Plant material of interest.
- General appearance
- Microscopic characteristics.
- Geographical distribution.
- Identity tests.

The packing and storage were included in British, French and Brazilian Pharmacopoeia. The natural order was included in Homoeopathic Pharmacopoeia of United States. The Method of preparation of Homoeopathic medicines should depend on the Crude drugs that had taken and standardisation of process of preparation of medicines. If any differences in the crude drugs and methods of preparation of medicines, safety issues may arise. In India, quantity of active alkaloids had not given but in other countries the alkaloid content of particular drug is mentioned [13].

2.3. QUALITY CONTROL ISSUES:

The quality, safety, efficacy of a drug must be in regulatory system and aims at providing the therapeutic value in respect of its identity and optimum quantity of therapeutically active constituents. The crude drugs from many sources are the questionable for the quality control in aspects of pharmacognostical, physico-chemical, microbiological and others, which must be regulatory according to the pharmacopoeial monographical standards. This is explained mainly in the Drugs and Cosmetics Act 1940. The purpose of this monographs is to prepare a Pharmacopoeia of Homoeopathic Drugs; to lay down principles and standards for the preparation of Homoeopathic Drugs; to lay down test of identity, quality, purity; and such other matters are incidental and necessary for the preparation of Homoeopathic Pharmacopoeia [13,15].

The natural biological and geographical variation of starting materials are an integral part of quality of homoeopathic medicines. It is standardised according to official homoeopathic pharmacopoeias and other officially recognised documents, and validated according to GMP.

The complex and variable nature of materials and its possible contamination with microbes, insects, pesticides, heavy metals, fumigants, mycotoxins and radioactive substance play an important role in manufacture of homoeopathic plant medicines [13,15].

As per the quality control issues for Homoeopathic medicines by WHO (2009), when using the plant material, including parts of plants, exudates or processed materials should satisfy the relevant national quality standards and specifications, pharmacopoeial analytical requirements and monographs, testing guidelines. Manufacturers are advised to follow exemplary standards and provisions regarding identification of source material, limit tests, and complementary tests [13].

The principles regarding identification of source material includes scientific name, stage of growth, part of plant used, information of cultivation and collection, macroscopic and microscopic characteristics, analytical determination of marker substances (if applicable). The limit tests should be done in regards of pesticides, contaminations, raw material, etc in Pharmacopoeial standards. Complementary tests includes the tests for foreign matter, total ash, water content, bitterness value, loss on drying and radioactive contamination. Apart from the preparation process, the mother tinctures, Finished products, Diluents and excipients, Impurities and contaminants also have some quality issues. The Finished product should comply the requirements such as identity and content, quality of dosage form, residual solvents, reagent or incidental contamination, stability test after the preparation process [13].

The Good Manufacturing Practices (GMP) of Homoeopathic drugs includes raw materials used in the manufacture of drugs are authentic, of prescribed quality, free from contamination, standard manufacturing process, acceptable qualitative manufactured drug ^[9]. The standardisation of Homoeopathic drugs is also established by the usage of sophisticated instruments such as high-performance liquid chromatography, high-performance thin-layer chromatography, fingerprinting and assays of marker compounds. It is again the consideration of scientificity by its authenticity and reproducibility and thereby developing the research aspects of Homoeopathy ^[17]. The evaluation of specification, linearity, precision, accuracy, LOD, Limit of Qualification, robustness and system suitability plays a role in validation of optimized chromatographic conditions ^[18].

The standardisation further have been explored the usage of licensed Homoeopathic medicines throughout the particular country. The licensed Homoeopathic Drugs in Germany is about 1235, whereas in Switzerland, a place with a simplified Product registration process, it

is about 12,000. So the standardisation starts from the licensing the product. Standardisation is necessary from proving to pharmacopoeias, manufacturing and dispensing [19].

In India, the Drug and Cosmetic Rules, 1945, has been continuously revising the rules and regulations for the preparation of drugs according to Pharmacopoeial reference. Since each consignment of the material shall be accompanied by a statement of the supplier's name; name of the plant with description of the part supplied; the Pharmacopoeial reference, place of collection, date of packaging and weight as instructed, the quality must be maintained [10].

<u>2.4. HARMONISATION EFFORT – UP TO DATE:</u>

The necessity for harmonization is expressed in following reviews.

2.4.1. INTERNATIONAL MEETING WORLD PHARMACOPOEIAS [2]:

Despite differences in language and medicines regulation among countries, internationalization principles to maintain quality of medicines should be established. Some complexity and diversity of most pharmacopoeias results from mutual integration and interdependence, with monographs for Homoeopathic preparations.

2.4.2. MEDICAL PLURALISM REGULATIONS: A PERSPECTIVE [16].

The identically entitled pharmacopoeial monographs have considerable differences. Since definitions may vary between pharmacopoeias, and because of wide range of processing techniques and manufacturing methods in various pharmacopoeias, the final homoeopathic products may show marked variability. The main homoeopathic pharmacopoeias being Pharmacopoeia Francaise, the German Homoeopathic Pharmacopoeia, the Homoeopathic Pharmacopoeia of United States and the HPI can give substantial inputs to each other for future growth of system. Harmonisation of monographs and convergence is recommended as future prospects for the development of system.

2.4.3. CHALLENGES FOR QUALITY CONTROL OF HOMOEOPATHIC MEDICINES [15]

With all the discrepancies, the pharmacy community is trying to develop a harmony or uniformity which will lead to avoid divergent future requirements through harmonisation of General Chapters, Monographs, Reference standards; to help drug regulators to assess quality on a common benchmark; to encourage the implementation and integration of common standards; to easier, faster and economical adoption of standards by manufacturers; to facilitate

the adoption of new or improved technical research and development approaches which update and replace current practices. The different standards and characteristics of different countries must be put into argument. The pharmacopoeial monographs have some differences of definitions, processing techniques and manufacturing methods and thereby final homoeopathic products show marked variability.

2.4.4. INTERNATIONAL CONFERENCE ON HARMONIZATION OF TECHNICAL REQUIREMENTS FOR REGISTRATION OF PHARMACEUTICALS FOR HUMAN USE [20]

The idea of harmonization was decided by many countries like Europe, Japan and United States, and conducted International Conference on Harmonization of Technical Requirements of Pharmaceuticals for Human Use in 1990 at WHO conference in Paris. It suggested the concept of Harmonization which helps to prevent the duplication and promotion of the safety and effectiveness.

2.4.5.THE HARMONIZATION PROCESS OF ICH. IN: PROCEEDINGS OF INTERNATIONAL CONFERENCE OF DRUG REGULATORY AUTHORITIES (ICDRA) [21]

The focus of Harmonisation has been mainly based initially on the risk analysis of pharmacovigilance activities such as pharmacological laboratories, regional or national centres for monitoring of adverse drug reactions and scientific publications. Harmonisation on the risk quantification should also be done to reduce the adverse reactions. This approach leads to the standards of quality, safety, and efficacy, improve drug availability and thereby to improve the standards of public health.

The Initiatives for the Harmonization effort were undertaken in many regions. But still the implementation is not yet started. Therefore, the countries should aim to implement while evaluating initiatives and to provide guidelines for strengthening regulations of the harmonization technique with the guide of World Health Organization ^[22]. The objectives of harmonization should be based on the assessment of safety and quality of the homoeopathic products, licensing the manufacturers and confirming it to GMP. The WHO should harmonize in many aspects such as definitions of homoeopathic products, cooperate the safety degrees of dilutions of Homoeopathic preparations, to promote the exchange of information through communication between the countries ^[23]. The process of Harmonization should have begun

with the drug proving in Homoeopathy with some aims to assist in understanding of basic structure and framework of drug proving, to comply scientific standards, to assist the various pharmacopoeias in their monograph approval process ^[24].

The Harmonization efforts in India had been initiated by sharing information among leading pharmacopoeias, providing quality medicines through harmonized drug standards and through effective regulatory systems. The WHO had decided to focus on international harmonization between world pharmacopoeias, international bank of harmonized texts for substances and finished dosage forms of the most common vital medicines, to build up frameworks for exchange of information, introduction of new techniques, analytical fingerprints, non-destructive spectroscopic methods and imaging.

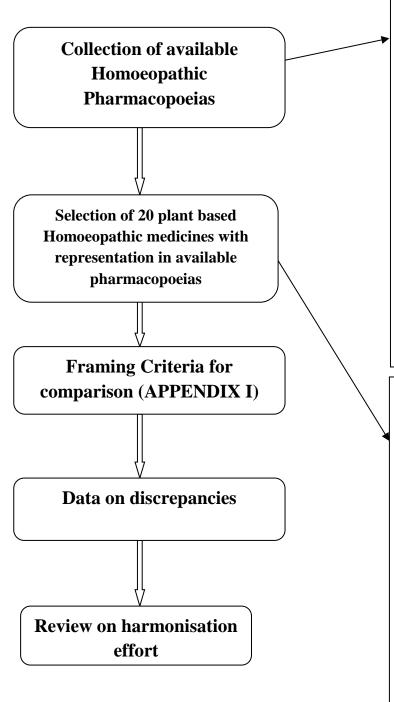
The reports and studies on pharmacopoeial standardisation suggest that the homoeopathic pharmacopoeias need to be harmonised and attempts to harmonise are taken place. This study aimed at understanding the discrepancies existing among the standard pharmacopoeias including 20 commonly used plant based medicines and to make a review on harmonisation attempts among the pharmacopoeias answering to the frequently asked questions like how to use the alternate procedures and interchangeable methods, whether a synthetic approach with all different methods will be applicable and whether all of them differ or equivalent from the works already done [15] in this direction. This study helps in providing the harmonization effort and which again helps in providing the standardization and quality control issues in the production of Homoeopathic Drugs. This study aims to result a review on current status of homoeopathic pharmacopoeias and attempts at harmonisation on the same.

3. OBJECTIVES:

- Comparison of Pharmacopoeial monographs on selected plant medicines from different pharmacopoeia and generate data on discrepancies.
- Review on harmonisation efforts on pharmacopoeias.

4. METHODOLOGY

• A Systematic review of pharmacopoeial monograph of 20 plant medicines.



LIST OF HOMOEOPATHIC PHARMACOPOEIA:

- 1. HOMOEOPATHIC PHARMACOPOEIA OF INDIA (HPI)
- 2. HOMOEOPATHIC PHARMACOPOEIA OF UNITED STATES (HPUS)
- 3. BRITISH HOMOEOPATHIC PHARMACOPOEIA (BHP)
- 4. GERMAN HOMOEOPATHIC PHARMACOPOEIA (GHP)
- 5. FRENCH HOMOEOPATHIC PHARMACOPOEIA (FHP)
- 6. BRAZILIAN HOMOEOPATHIC PHARMACOPOEIA (Br HP)
- 7. MEXICAN HOMOEOPATHIC PHARMACOPOEIA (MHP)

LIST OF 20 PLANT BASED MEDICINES:

- 1. ACONITUM NAPELLUS
- 2. AESCULUS HIPPOCASTANUM
- 3. AETHUSA CYNAPIUM
- 4. ALLIUM CEPA
- 5. ALLIUM SATIVUM
- 6. ARNICA MONTANA
- 7. ASAFOETIDA
- 8. AVENA SATIVA
- 9. BELLADONNA
- 10. CALENDULA OFFICINALIS
- 11. CHELIDONIUM MAJUS
- 12. CYCLAMEN EUROPAEUM
- 13. GELSEMIUM SEMPERVIRENS
- 14. HYOSCYAMUS NIGER
- 15. HYPERICUM PERFORATUM
- 16. LYCOPODIUM CLAVATUM
- 17. NUX VOMICA
- 18. RHUS TOXICODENDRON
- 19. THUJA OCCIDENTALIS
- 20. UVA URSI

5. DATA ON DISCREPANCIES:

5.1. ACONITUM NAPELLUS:





Synonyms:

- In Mexican Homoeopathic Pharmacopoeia, the synonym is presented under the title of different languages e.g., Latin, Spanish.
- There is no synonym mentioned under British Homoeopathic Pharmacopoeia & Brazillian Homoeopathic Pharmacopoeia.

Description:

- Morphology of root is well described under French Homoeopathic Pharmacopoeia.
- Flowering months are described as May to July in Homoeopathic Pharmacopoeia of India & Mexican Homoeopathic Pharmacopoeia.
- There is no description about root on German Homoeopathic Pharmacopoeia & Homoeopathic Pharmacopoeia of India.
- In Homoeopathic Pharmacopoeia of United States, root is mentioned as tapering where as in French Homoeopathic Pharmacopoeia, it is explained of having a lozenge-shape bearing secondary roots together with tuber-root daughter.

Part used:

- In general WHOLE PLANT is used for the medicinal preparation. Fresh blooming plant is also another point taken in to consideration.
- In German Homoeopathic Pharmacopoeia, it is specified whole plant except root
- In Mexican Homoeopathic Pharmacopoeia, whole plant & its root, harvested at beginning of flowering (because the alkaloid aconitine is released more at flowering season).

Preparation:

• In general, mother tincture with a drug strength of 1/10 is specified, 3X and higher is recommended for medication.

- French Homoeopathic Pharmacopoeia describes the preparation in a vague manner when compared to Homoeopathic Pharmacopoeia of United States, Homoeopathic Pharmacopoeia of India & Mexican Homoeopathic Pharmacopoeia.
- There is no preparation in German Homoeopathic Pharmacopoeia, Brazillian Homoeopathic Pharmacopoeia & British Homoeopathic Pharmacopoeia.
- In Mexican Homoeopathic Pharmacopoeia, dispensing alcohol is noted as "officinal alcohol".

Identification:

- It is well explained under HPI & FHP. Thin Layer Chromatography is used for identification of phytochemicals.
- Detailed explanation of each phases of TLC is explained in FHP.

History & Authority:

- Explained in HPI, HPUS, MHP.
- Hering.C Guiding Symptom is pointed out only under HPI.

5.2.AESCULUS HIPPOCASTANUM:





Synonyms:

- It is explained language wise in HPUS (Latin and English) and MHP (Latin and Spanish).
- There is no synonym mentioned under BHP & GHP.

Description:

- June is specified as the following month in HPI & MHP.
- In FHP, the morphology of seed is well explained.
- Even though the seed is used for the preparation of medicine, its morphology is not explained in HPUS, BrHP, GHP, BHP.

Part used:

- Often ripe nut excluding the order shell is used for preparing medicine.
- But in BrHP, dry shelled seed & ripe, fresh, shelled walnut is recommended respectively.

Preparation:

- In HPI, under trituration 1X higher can be used. In this, it is also explained that 6X may convert to liquid 8X, 9X & higher with dispensing alcohol.
- In BrHP, it is explained that maceration/ percolation in which the alcohol strength during/ by the end of extraction is 65% (v/v).

Identification:

History & Authority:

• Even though the medicine is proved is introduced by Helbig in 1844, it is not mentioned in HPI.

5.3.AETHUSA CYNAPIUM:



Synonym:

- It is mentioned language wise in HPI (English, French, German); HPUS (English, French, German); MHP(Latin and Spanish)
- There is no synonym mentioned under BHP & Brazillian HP.

Description:

- The flowering months of the plant was well explained in MHP as July to September.
- In FHP, the morphology of flower in well explained
- Foetidness of leaves is commonly explained in all pharmacopoiea except BHP & Br HP.

Part used:

• In MHP, Whole fresh plant which is fully flowered is specifically mentioned.

• In general whole fresh plant is mentioned.

Preparation:

• Potencies apt for the purpose of medication is explained in HPUS i.e, 3X and higher.

Identification:

History and Authority:

• In HPUS, along with the prover to the details of published, it give details on the derivation of name.

5.4.ALLIUM CEPA:



Synonym:

- In HPUS and Mexican HP synonym is mentioned in Latin and English and Latin and Spanish respectively.
- In Brazilian HP "family Liliacea" is mentioned

Description:

• In HPI plant is described as perennial where as in Mexican HP it is mentioned as biennial

Preparation:

- In HPUS and Mexican HP plant moisture(100 g of magma) is mentioned 567 cc
- Specification for the preparation of mother tincture from 1CH TO 3 CH / 1 DH to 6 DH I is mentioned in Brazilian HP.

Identification:

• Explained in Mexican HP – various experiment along with TLC

5.5.ALLIUM SATIVA:



Synonym:

- Synonym is given in Latin and English in HPUS and Mexican HP it is mentioned in Latin and Spanish.
- Radices S. Bulbi is only found in GHP.
- There is no synonym in FHP ND Brazilian HP.

Description:

• Flowering months (June to July) is only mentioned HPUS and Mexican HP

Part used:

- In GHP fresh bulb without membrane an essence of garlic is mentioned.
- In Mexican HP the months are specified for collecting the fresh bulb (June, July, August)

Preparation:

• In GHP "the essence of flowers after rule 2" is mentioned.

5.6.ARNICA MONTANA:



Synonym:

• Given language wise in HPI, HPUS, Mexican HP.

Description:

- In HPUS and in Mexican HP moths of flowering is specified (July to August)
- In GHP the root is thick and quill running slanting end bitten very ;Long and fleshy fibrils , where as in Mexican HP the roots are thread like.
- In FHP leaves speciality "secretory trichomes" is mentioned.
- Well explained in Brazilian HP.

Part used:

- Generally whole plant is used.
- In FHP entire fresh blooming plant is used.
- In Brazilian HP drug plant is used.
- In BHP whole plant generally dried rhizome and rootlets arte used.

Preparation:

• In HPUS mother tincture of entire plant including the root (class C/ class N).

5.7. ASAFOETIDA:



Synonym:

- Language wise given in HPUS (Latin, English and French)
- FHP, Brazilian HP and Mexican HP there is no synonym.

Description:

- In HPI its morphology is well described. It is correctly specified as "oleogum resin". The 3 forms (paste, tears, mass), two varieties [F.foetida and F.rubriculis] and the notes on their part is defined.
- In HPI and GHP the colour changes undergone when exposed to open air is explained.
- HPUS method of purification in mechanical way along with solubility.
- BHP is vaguely described.

Preparation:

- Potency is specified only in HPI -2X and higher with dispensing alcohol.
- GHP mother tincture is made with the strong spirit of cohine. after Rule 1.
- BHP mother tincture is prepared using rectified spirit.
- HPUS class E is mentioned.

Identification:

- In GHP physical characteristics are used.
- In HPI –TLC.

- Only given in HPI and BHP.
- HPI proved by Franz in 1822 along with source books.
- BHP reference to homoeopathic drug proving.

5.8. AVENA SATIVA:





Synonym:

- In HPI the synonym is Hindi, English, French, German is used.
- In HPUS English, French, German synonym are mentioned.
- In Mexican HP Latin, Chinese and Spanish names are given.

Description:

• Description of fruit is given only in Brazililan HP.

Part used:

- In HPI whole plant is used.
- In HPUS,FHP,Brazilian HP fresh aerial part of flowering plant.
- In Mexican HP –fresh seeds.

Preparation:

- Maceration time (3 to 5 weeks) is explained only in FHP.
- Even though part used section Mexican HP explained it as fresh seeds when it comes to preparation it explains the fresh whole plant.

- In Mexican HP- explains about the environmental conditions at which it can be cultivated but the prover is not explained.
- In HPI Clarke .J.H. is the prover.

5.9. BELLADONNA:



Synonym:

• In HPUS the synonyms in Latin, English, French and German is mentined.

Morphology:

- GHP the native of the plant is mentioned –Germany
- HPUS flowering months (august,may).
- In Brazilian HP reason for tiny shiny clots in leaves is explained due to microcrystalline content of calcium oxalate in mesophyll.

Part used:

- In general whole plant is used.
- In HPUS and Brazilian HP –specified when beginning to flower.
- In GHP leaves especially those near roots and he lower of the stem.

Identification:

- In HPI –TLC.
- In GHP Physical properties.
- In Brazilian HP –chemical lab tests.

- In BHP-reference to Hom . proving –R.A.M.L.
- In HPI-T.F.Allen Encyclopedia.

5.10.CALENDULA OFFICINALIS:



Synonym:

- In HPUS –English.
- In Mexican HP Latin and Spanish.

Description:

• In HPUS and in Mexican HP the nature of flowering is detailed, it flower during most of the summer and fall, flowers closes at night.

Part used:

- In general flowering tops.
- In HPI, GHP, BHP along with flowering tops leaves are mentioned.

Identification:

- In HPI –TLC.
- In GHP-physical properties.
- In Brazilian –chemical tests.

- In HPI AND Mexican HP provers name is mentioned.
- Franzen in MHP;1838.but in HPI 'franz'

5.11.CHELIDONIUM MAJUS:



Synonym:

- HPUS –Latin,English,German.
- MHP- Latin and Spanish.

Description:

- In HPUS it is mentioned as biennial plant where as in other pharmacopoeia it is mentioned as perennial.
- In HPUS flowering march to august.
- In MHP-flowering –may to October.

Part used:

- In general whole plant.
- In GHP –root dug.
- In Brazilian HP and MHP along with whole plant –root is specified.

- In HPI and MHP- prover Hahnemann.
- In GHP –physical properties.

5.12.CYCLAMEN EUROPAEUM:





Synonyms:

- In HPUS Latin ,French,German.
- In MHP Latin ,Spanish.

Morphology:

• In HPUS –Flowers of summer.

Part used:

- Root in general.
- In GHP –roots are gathered during autumn before second flower.
- In MHP –fresh root harvested in autumn.

Preparation:

• In HPI- Potencies where as an MHP –dynamization.

Identification:

- In GHP-physical property.
- FHP-TLC.
- Brazilian HP- chemical test.

History and Authority:

• In HPI and MHP- Hahnemann's name is specified.

5.13.GELSEMIUM SEMPERVIRENS:





Synonym:

- HPI-English, French, German.
- HPUS-Latin, English, French, German.
- MHP-Latin and Spanish.

Morphology:

- HPUS flowering march and april.
- Brazilian HP-detailed study microscopic studies-rhizome.
- MHP-march to april.
- Brazilian HP –perennial shrub.

Part used:

- FHP- dried under ground part.
- Brazilian HP- rhizome and dry root.
- MHP-fresh root.

Identification:

- FHP- TLC.
- Brazilian HP chemical test.

- HPI-proved by Douglas.
- MHP-he mentioned in homoeopathic literature Dr. Mefcalfe in 1853.

5.14.HYOSCYAMUS NIGER:



Synonym:

- HPI-Hindi, English, French, German.
- HPUS- Latin, English, French, German.
- MHP-Latin.

Description:

- HPUS and MHP -flowering –june to august.
- HPUS and MHP-long haus in stem tiped with a minute black gland (offensiveness).

Part used:

- HPI-whole plant of 2nd year growth.
- GHP-laves in flowers branches after removing the ligneous stem
- Brazilian HP-whole flowered dry plant.
- MHP-Florida, fresh whole plant collected the 2nd year of growth.
- BHP-Herbaceous part of the plant.

Identification:

- HPI-colour test and TLC.
- Brazilian HP-Lab test and TLC.

History and Authority:

• HPI and MHP-Hahnemann introduced.

5.15.HYPERICUM PERFORATUM:



Synonym:

- HPUS Latin, English, French, German.
- MHP-Latin and Spanish.

Description:

- GHP-NATIVE –Europe and near edges of woods in ditches, near roads and balks and upon sunny hills.
- Brazilian HP-fruits have aromatic and persistent odour ,better and astringent flavor.
- MHP-due to intense balsamic order of the plant it is called noxious weed.
- BHP-black oil glands in the margins of seplas.

Part used:

• In Brazilian HP and MHP-whole flowering plant.

Preparation:

• In MHP- for preparing potencies –for Hahnemann preparation rule 3 is suggested.

History and Authority:

• Only explained in MHP-Hom. Practice introduced by Dr.Muller Experimentation.

5.16.LYCOPODIUM CLAVATUM:



Synonym:

- HPI-Hindi, English, French.
- HPUS-English, French, German.
- MHP-Latin, Spanish.

Description:

- No Description was given in the BHP.
- In MHP, Specification of flowers blooming in July to August.
- In HPI & BrHP, perennial type is mentioned.

Part used:

- In BHP- spores wrongly called pollen/seeds.
- In HPUS –class C and F are mentioned in preparation of tincture.
- In MHP-for Hahnemannian preparation rule 4 and 7 are used.

Identification:

- In HPI –TLC.
- In Brazilian HP- chemical tests

History and Authority:

• Only in HPI and MHP-Hahnemann.

5.17. NUX VOMICA:



Synonym:

- In HPI-Latin, English, French, German.
- In HPUS- Latin, French, German.
- In GHP-Latin, German.
- In MHP-Latin, Spanish.

History and Authority:

- In HPI, MHP- prover -Hahnemann.
- In BHP-reference to Homoeopathic Proving -R,A,M,L,i.

Description:

- Even though part used is seed it is not mentioned in FHP, BHP, HPI.
- In FHP nothing is explained.

Part used:

- In BHP-dry seeds.
- In MHP, BHP, HPI-seeds.
- In HPUS, GHP, FHP-not mentioned.

Preparation:

- In GHP-preparation after rule-1.
- In Brazilian HP- Prepared by maceration and percolation and alcoholic content at the end of extraction is 65% v/v.
- In MHP-Preparation by dynamization following with officinal alcohol, Hahnemannian preparation by Rule 4, Rule 7.
- In HPI-potencies 2 X and higher with dispensing alcohol.

5.18 .RHUS TOXICODENDRON:



Synonym:

- In HPI-Latin, English, German.
- In HPUS-Latin, English, French.
- In FHP- Latin.
- In MHP-Latin, Spanish.
- In BHP- English, French.

History and Authority:

• Mentioned only in HPI and MHP-Introduced and proved by Hahnemann.

Description:

- In HPUS- Mentioned as perennial shrub.
- In HPI-Roots are described as thin aerial roots.
- In GHP-Flowering season is mentioned from june to august.
- In MHP-Flowering in june.

Part used:

- In BHP-part used is specifically mentioned it as collected at night and never exposed to sun.
- Not mentioned in HPUS and GHP.
- Fresh leaves in MHP and FHP.
- Leaves in Brazilian HP and HPI.

Preparation:

- In HPI-Potencies 3 X and higher with dispensing alcohol.
- In HPUS-tincture of leaves is mentioned but mentioned in part used.
- In FHP-Tincture is prepared with ethanol.

- Though it introduced and mentioned by Hahnemann no preparations or other things are mentioned in GHP.
- In Brazilian HP –preparation is by maceration and percolation.
- In MHP- dynamization for preparation, and Hahnemannian preparation –rule 3.
- In BHP-tincture prepared using proof spirit.

Identification:

• Only In HPI, BHP- TLC.

5.19. THUJA OCCIDENTALIS:



Synonym:

- In HPI-Latin, English, French, German.
- In HPUS-Latin, English, French, German.
- In MHP-Latin, German.

History and Authority:

• In HPI-Mentioned in HERING.C .GUIDING SYMPTOMS,1879,10,306.

Description:

- In FHP of part is there.
- In MHP-Leaves are not mentioned.
- In MHP and HPUS-Flowering is may and june.

Part used:

- Fresh leaves in MHP.
- In FHP and HPUS not mentioned.

Preparation:

- In HPI-2 X and higher with dispensing alcohol.
- In GHP-Tincture is prepared after rule-3.
- In Brazilian HP-maceration and percolation, 2X Following officinal alcohol.
- In MHP-dynamization and Hahnemannian preparation is after rule-2.

Identification:

• In HPI and Brazilian HP-TLC.

5.20. UVA URSI:



Synonym:

- In HPI-Latin, French, English, German.
- In HPUS- Latin, English, French.
- In MHP-Latin, Spanish.

Description:

- MHP-Flowering is may.
- In GHP-Leaves gathered about autumn contain much tannin making iron blue the characteristic distinguishing them from similar leaves.
- In MHP- Root –small with thick bush.

Part used:

• Only mentioned in HPI, MHP, BHP-Fresh leaves.

Preparation:

• HPI-2X and higher with purified water.

- 3X and higher with dispensing alcohol.
- HPUS-Tincture of leaves CLASS C/ CLASS M.
- In MHP-Hahnemannian after rule-2

Identification:

• Only mentioned in HPI-TLC.

History and Authority:

- In HPI-Mentioned as proved by Hahnemann, Heberdon, Noack, Trincks, Mitchel, sauvages, Essay, Bartam.
- In BHP-Ref-to Hom.proving.Noack and Trincks.

6. AN OVERVIEW OF DATA ON DISCREPANCIES:

Discrepancies are considered under many aspects like Synonyms, Description, Parts used, Preparation, Identification, History and Authority.

6.1. SYNONYMS:

Synonyms has been used in different languages in MHP (Latin & Spanish); HPUS (Latin & English) and HPI. In Pharmacopoeias like BHP, Brazillian HP, GHP, FHP, MHP, there are no synonyms has been mentioned for few drugs. For example, In MHP, Asafoetida has no synonym but synonyms has been given for Aethusa cynapium.

6.2 DESCRIPTION:

Description should be explained specifically for the differentiation of sub species. Every pharmacopoeia is unique in its own aspects.

In some pharmacopoeias the morphology of parts used for preparation of medicine
has not been explained. For example, seed of Aesculus is not been explained in
HPUS, Brazillian HP, GHP. BHP though seed is the main source of preparation of
medicine.

6.3. PARTS USED:

Parts used is an important point to deal when we are comparing the pharmacopoeias.

- In this section, the lot of the discrepancies like usage of different parts for the preparation. For e.g. In Aconitum napellus, some have whole plant and some have whole plant except root and other have whole plant with root and In Calendula officinalis part used is given as flowers and leaves in HPI, GHP,BHP. But Only flowers in HPUS, BrHP, MHP.
- Further, the harvesting period has been given in some pharmacopoeia. For e.g, Aconite in MHP and HPUS, Cyclamen in GHP.
- Some pharmacopoeias give the nature of the part used dry / fresh plant. There are many differences present. For e. g, Arnica Montana in FHP (fresh), Brazillian HP (dry), and BHP (dried).

6.4. PREPARATION:

It explains mainly the preparation of the medicines in various forms.

- In general, different terms were used in various pharmacopoeias. For e.g, various terms like officinal alcohol instead of dispensing alcohol in MHP.
- FHP describes the preparation in a vague manner, when compared to HPI, HPUS and MHP.
- Some has given with dynamization techniques. For e.g., In HPI, tincture, potencies, trituration were described. In HPUS, tincture, dilutions, medications, trituration were described. In MHP tincture, dynamization, trituration, were described.
- Some pharmacopoeias have given the drug strength and others with the components of mother tincture Tincture preparation is only given in the GHP. Step by step procedure of tincture preparation is given in BrHP.

6.5. .IDENTIFICATION:

It is the step to analyze quantitatively, the prepared medicine in mother tincture form. The chromatographic techniques were used widely for this.

- Thin layer chromatography (TLC) and paper chromatography (PC) were used in HPI.
- Brazilian HP explains detailed about the identification process under many methods and finally with Thin Layer Chromatography.

- Detailed explanation of Thin Layer Chromatography is given in HPI and FHP.
 Further in FHP, the detailed step by step phases were elaborated.
- In GHP, physical characteristics of the plant like smell and microscopic appearance is given in this section.
- This section is not dealt in HPUS, MHP, BHP.

6.6. HISTORY AND AUTHORITY:

History and Authority provides the evidences for proving of all medicines.

- It was given in HPI, BHP, HPUS, MHP. While others have no such Authority.
- HPI is given with Encyclopedia of Pure Materia Medica by T.F.Allen, Dictionary of practical Materia Medica by J.H.Clarke, Herings Guiding symptom of Materia Medica, and Materia Medica Pura, etc.
- BHP have some References to Homoeopathic Proving but not well explained.
- HPUS have some history and no clear explanation is given.

7. CONCLUSION:

It is found that the detailed explanation about each drug in all aspects like Synonyms, Description, Parts used, Preparation, Identification, History and Authority has been given in monographs of all pharmacopoeias. Some pharmacopoeias lack some medicines that are broadly discussed in other pharmacopoeias. On comparison, there are many discrepancies and similarities found in all drugs. The main aspect of dissimilarity exists in the Synonyms, Parts used and Preparation of medicine. This further leads to variations in the quality control issues in the patient care and in the standardisation of preparation of drugs. Due to these discrepancies, discussions were made in some International conferences for the implementation of effective standardisation in preparation of drugs and thus further evaluation is needed in Pharmacopoeias for standardized Homoeopathy.

6. REFERENCES:

- Kumar, S. (2015). Herbal Pharmacopoiea an overview of International and Indian representation. [online] Ayurvedjournal.com. Available at: http://www.ayurvedjournal.com/ JAHM_201513_01.pdf [Accessed 31 Jul. 2018
- 2. Who.int. (2012). [online] Available at: http://www.who.int/ medicines /areas/quality_safety/quality_assurance/resources/InternationalMeetingWorldPharmac opoeias_QAS13-512Rev1_25032013.pdf [Accessed 31 Jul. 2018]..
- 3. Ayush.gov.in. (n.d.). [online] Available at: http://ayush.gov.in/ sites/ default/files/ Ayurvedic%20Pharmacopoeia%20of%20India%20part%201%20volume%20IX.pdf [Accessed 31 Jul. 2018].,
- 4. Ayush.gov.in.(2016).[online] Available at: http://ayush.gov.in/ sites/default/files/Unani%20Pharmacopoeia%20of%20India%20Part%20II%20Vol%203.p df [Accessed 31 Jul. 2018].
- 5. Nischennai.org. (n.d.). [online] Available at: http://nischennai.org/uploaded/pdf/THE%20SIDDHA%20PHARMACOPOEIA%20OF%20INDIA.pdf [Accessed 31 Jul. 2018].,
- 6. Overview of Updated Chinese Pharmacopoiea [Internet]. Edqm.eu. 2016 [cited 1 August 2018]. Available from: https://www.edqm.eu/ sites/default/files/1710_0915_overview_of_chinese_pharmacopoeia_commission_chpc_up date_of_chinese_pharmacopoeia_chp-en.pdf
- 7. Tiwari, L., Rai, N. and Kr Sharma, R. (2013). Regulatory Standards on Homoeopathic Drugs: Indian Perspective. International Journal of Advanced Pharmaceutical Science and Technology, [online] 1(1), pp.1-20.Availableat:http://scientific.cloudjournals.com/index.php/IJAPST/article/view/Sci-72 [Accessed 31 Jul. 2018].
- 8. Das, E. (2018). Chronology of literature related to Homoeopathic Pharmacopeia | National Health Portal of India. [online] Nhp.gov.in. Available at: https://www.nhp.gov.in/chronology-of-literature-related-to-homoeopathic-pharmacopeia_mtl [Accessed 31 Jul. 2018].
- 9. Ayush.gov.in. (2018).Guidelines for Inspection of GMP Compliance by Homoeopathic Drug Industry. [online] Available at: http://ayush.gov.in/sites/default/files/8536171420Guidelines%20For%20Inspection%20Of%20GMP%20

- Compliance%20By%20Homoeopathic%20Drug%20Industry%20%20%2012.pdf [Accessed 31 Jul. 2018].].
- 10. Ayush.gov.in. (2017). Homoeopathy Amendment of Drugs and Cosmetics Rules. [online] Available at: http://ayush.gov.in/ sites/ default/ files/HomoeopathyAmendnment%20of%20Drugs%20and%20Cosmetic%20Rules_0. pdf [Accessed 1 Aug. 2018].
- 11. Chen X, Xiang L, Shi L, Li G, Yao H, Han J et al. Identification of crude drugs in the Japanese pharmacopoeia using a DNA barcoding system. Scientific Reports. 2017;7(1).
- 12. .Homoeopathic Pharmacopoiea of India Volume-1 [Internet]. Ccrhindia.nic.in. 2016 [cited 1 August 2018]. Available from: http://ccrhindia.nic.in// admnis/ admin/ showimg.aspx?ID=12536]
- 13. Safety issues in the preparation of Homoeopathic medicines [Internet].Quality control issues for Homoeopathic medicines. who.int. 2009 [cited 2 August 2018]. Availablefrom:
 - http://www.who.int/medicines/areas/traditional/Homeopathy.pdf?ua=1
- 14. Mandal PP, Mandal B. A Textbook of Homoeopathic Pharmacy.3rd ed. Kolkata :New Central Book Agency(P) Ltd;2014.p.1-9.
- 15. Safety issues in the preparation of Homoeopathic medicines [Internet]. Challenges for Quality control of Homoeopathic medicines. who.int. 2009 [cited 2 August 2018]. Available from: http://www.who.int/medicines/areas/traditional/Homeopathy.pdf?ua=1
- 16. Manchanda RK. Medical Pluralism,regulations: APerspective. Indian J Res Homoeopathy (2017); 11(2): 85-7. Available from: http://www.ijrh.org/article.asp?issn=0974-7168.
- 17. Manchanda RK. Popularity, safety and quality of homoeopathic medicines. Indian J Res Homoeopathy 2018;12:191-3. DOI: 10.4103/ijrh.ijrh_72_18.
- 18. Goswami N. A validated stability- indicating liquid chromatographic method for determination of process related impurities and degradation behavior of Irbesartan in solid oral dosage. J Adv Pharm Technol Res 2014;5:33-40. DOI: 10.4103/2231-4040.126985.
- 19. Kaur H. Chaudhary Khurana A, HooverT, van Haselen R, A, medicine forum on Manchanda RK. World integrated the regulation of homoeopathic medicinal products: National and global strategies. Indian J Res Homoeopathy 2017;11:123-35.
 - Available from: http://www.ijrh.org/text.asp?2017/11/2/123/207662.

- 20. Singh J. International conference on harmonization of technical requirements for registration of pharmaceuticals for human use. J Pharmacol Pharmacother 2015;6:185-7. DOI: 10.4103/0976-500X.162004.
- 21. Hayashi Y. The Harmonization process of ICH. In: Proceedings of International Conference of Drug Regulatory Authorities (ICDRA) [conference proceedings on the Internet]; 2002 June 24-27; China. The Government of The People's Republic of China and World Health Organisation.
- 22. Matsoso MP. Regional Harmonization Initiatives. In: Proceedings of International Conference of Drug Regulatory Authorities (ICDRA) [conference proceedings on the Internet]; 2002 June 24-27; China. The Government of The People's Republic of China and World Health Organisation.
- 23. Shweim HG. Homoeopathy. In: Proceedings of International Conference of Drug Regulatory Authorities (ICDRA) [conference proceedings on the Internet]; 2002 June 24-27; China. The Government of The People's Republic of China and World Health Organisation.
- 24. Galassi R, Peinbauer T. *Homoeopathic Proving Guidelines*. Europe. Liga Medicorum Homoeopathica Internationalis and European Committee for Homoeopathy. Mgy 2014.
- 25. World Health Organisation. QAS/12.512/Rev.1. *International Meeting of World Pharmacopoeias*. Geneva: WHO; 2012.
- 26. World Health Organisation Monographs on selected Medicinal Plants [Internet]. 1999 [cited2019May28]. Available from:
 - https://apps.who.int/medicinedocs/en/d/Js2200e/5.html

A	P	P	\mathbf{E}	N	D	T	X	I:

COMPARISON CHART:

CRITERIAS	НРІ	HPUS	FHP	GHP	BRAZILIAN HP	MEXICAN HP	ВНР
SYNONYM							
DESCRIPTION							
IDENTIFICATION							
PART USED							
PREPARATION							
HISTORY AND AUTHORITY							