International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 25-04-2023, Accepted: 11-05-2023, Published: 26-05-2023
Volume 8, Issue 2, 2023, Page No. 98-104

Scope for harmonisation of herbal medicine regulations: Review

Shinde Pranjali[1*], Amrata Mantri[2], Dr. Dhananjay Ghodake[3], Dr. Rajendra Patil[4]
[1] Student, Delonix Society's Baramati College of Pharmacy, Barhanpur, Tal–Baramati Asaheb Ambedkar Technological University Lonere, Maharashtra, India
[2] Assistant Professor of Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati. Dr. Babasaheb Ambedkar Technological University, India
[3] Professor of Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati. Dr. Babasaheb Ambedkar Technological University, India
[4] Principal of Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati. Dr. Babasaheb Ambedkar Technological University, India

Abstract
As individuals become more conscious of lifestyle diseases and poor eating practises, herbal medicinal products are becoming more and more popular. Growing interest in self-care in the second half of the 20th century led to a huge increase in the acceptance of conventional treatment approaches, including the use of herbal remedies. Consumers are turning to herbal medicines and their supplements due to side effects from taking modern medications, which is fueling the global rise of herbal medicines. When offered for sale commercially, herbal medicines must adhere to local laws governing their efficacy, safety, and quality. The laws governing herbal medicines currently vary by nation. Companies that produce herbal medicines are unable to produce a uniform product for the worldwide market as a result. Thus, a coordinated effort should be made.

Keywords: herbal medicine, herbal medicines, worldwide market

Introduction [1, 2, 3, 4, 5]

Since ancient times, India has produced and marketed herbal medications under the names Ayurveda, Siddha, and Unani, among others. Herbal remedies are currently employed as an alternative to the allopathic medical system and for the prevention and treatment of illnesses as a result of consumer acceptance. Herbal remedies are already a crucial component of patient healthcare, so as global awareness of the benefits of their use increased, so did demand for herbal remedies as well as its commercialization. Globally, the abrupt rise in the use of herbal medicine raised questions about its efficacy, safety, and quality, necessitating the implementation of strict laws for its management. Innovative methods such as genetic sequencing, fingerprinting, active compound identification, authentication, and manipulation of biosynthetic processes resulted in the creation of novel drugs with increased clinical efficacy and decreased negative effects. By developing appropriate policies, standardising classification, enacting legislation to protect intellectual property, and enhancing pharmacovigilance, regulatory agencies of the member countries and WHO are aiming to establish a harmonised legislation for herbal medicines. ASEAN and nations including the United States, Canada, and the United Kingdom (UK), as well as EU members, already have well-established rules for herbal medicines, and they are now working with WHO to establish a standard framework for herbal medication regulation.

An Overview of Herbal Regulations across India, USA and EU India [6, 7, 8, 9, 10]

The Drug and Cosmetic Act (D and C) 1940 and Rules 1945, which contain provisions for the regulation of Ayurveda, Unani, and Siddha medicine, govern herbal medicines in India. Additionally, it provides for the regulation of the manufacture, formulation, labelling, packaging, and export of herbal medicines as well as their quality and content. Herbal medicines are regulated by the Department of AYUSH and it mandates that any manufacturing or marketing for herbal drugs has to be done only after completion of approval of the application for a license to manufacture the specified herbal medicine. Good manufacturing practice requirements for the manufacture of herbal medicines are laid down in the Schedule "T" of the D and C act.

Rules, Regulation & Governing Body in India

The Indian government officially recognised the Traditional Indian System of Medicine (ISM) in 1959, and the Drug and Cosmetic Act was updated to reflect this. The first of these expert working groups (EWG) was established in 1962, and over time, numerous EWGs for various ISM were swiftly formed. Act 13 of 1964 established a separate chapter for medications used in Ayurveda, Siddha, and Unani practises. The statute had several modifications in the years 1983, 1987, 1994, and 2002. Under the D and C Rules 1945, guidelines for the evaluation and analysis of pharmaceuticals were released in 2006 and 2008. The Central Council of Indian Medicine (CCIM) was established in 1970 and developed and executed several laws as well as the curricula and ISM (Ayurveda, Siddha, and Unani). The Sowa Rigpa medical system was integrated into the CCIM in 2012. The Department of Indian Medicine and Homoeopathy (ISM & H) was established in 1995 to advance ISM. In 2003 and 2014, it underwent a name change to become the Department of Ayurveda, Yoga, Naturopathy, Unani, Siddha, and Homoeopathy (AYUSH). The Department of AYUSH developed a certification

programme for AYUSH medicine goods in 2009 in partnership with QCI. Concerns regarding the effectiveness, safety, and calibre of AYUSH products have been voiced for a while. To address these issues, a new programme for the voluntary certification of AYUSH products in conjunction with QCI has been launched. The certification scheme offered by the AYUSH department comprises two levels. The first is called AYUSH Standard Mark, and it adheres to domestic regulatory standards. The second is called AYUSH
Premium Mark, and it combines the following possibilities; Option A: It should adhere to the
GMP specifications and levels of pollutants based on the WHO Guidelines listed in the Certification Criteria document. Option B: In contrast to Option A, which states that it must adhere to the legal requirements of any importing nation, Option B is stricter.

Ayush and Health Policy

The Department of AYUSH [36] in India focuses on governance in general, ISM growth, regulation, development, and education. These are made up of a number of independent organisations and a select number of supporting departments, including national institutions, research councils, academies, professional councils, pharmacopoeia laboratories, and hospitals. In 2002, a national policy on homoeopathy and Indian medical systems was unveiled. The main goal of this strategy is to use AYUSH to achieve excellent health and to promote healthcare to the public in the form of safe and efficient services and medications that adhere to pharmacopoeial standards and are of the same high calibre0 as AYUSH goods.

There are many legislative and administrative procedures in India to regulate the production and distribution of Ayurveda, Siddha, and Unani (ASU) medicine. In chapter IVA of the pharmaceuticals & Cosmetics Act of 1940, guidelines for the production, packaging, labelling, and selling of ASU pharmaceuticals were set down. Periodic updates are necessary for the evolution of ASU medicines; the most recent ones to this chapter IVA were made in March 2013.

Ayurveda, Siddha, and Unani Technical Advisory Board (ASUDTAB) was created specifically to address and advise the authorities on the technical issues related to the regulation of ASU medications. The Ayurveda, Siddha, and Unani Drugs Consultative Committee (ASUDCC) was established in India to comply with the 1940 Drugs & Cosmetics Act's administration. The Council for Scientific & Industrial Research (CSIR) laboratories and the Central Council for Research are responsible for ensuring the safety and quality of polyherbal / herbomineral formulations.

United States of America [11, 12, 13, 14, 15, 16]

In the US, the Dietary Supplement Health and Education Act (DSHEA) of 1994 designated herbs as dietary supplements.

In contras occur without a safety and efficacy profile. In accordance with the FDA's standards, dietary supplements that are deemed unsafe for ingestion can be taken off the market. Before the producer releases the dietary supplemet to pharmaceuticals, the production, marketing, and sale of dietary supplements nt into the market, the FDA needs to see proof of its efficacy and safety. There are two categories of herbal drug products: over-the-counter (OTC) and those that need New Drug Applications (NDAs) that have been reviewed by CDER of the USFDA.

Drugs made from plants are marketed as completed herbal remedies and incorporate plant elements as ingredients. After receiving NDA, ANDA, or counter product approval, these products are then marketed. According to 21 CFR sections 331-358 of FDA regulations, a herbal drug product is qualified for inclusion in the OTC drug monograph if it has been sold for a long time for a particular indication. If a manufacturer of herbal drug products wants to change a monograph to add a new herbal substance, per 21 CFR 10.30, a petition must be filed.

Any person may market the same product even if it contains the same ingredient and is used for the same indication after the publication of the final OTC drug monograph for a specific herbal drug product with regard to a specific indication. However, the requirement that the labelling and another active component be submitted by the person still stands. If a new herbal drug product is approved through an NDA, the USFDA will provide the drug developer a market exclusivity period of five years beginning on the date of approval even in circumstances where there is no patent protection.

A novel herbal medication that has numerous chemical components is qualified to be referred to as a new chemical compound under 314.108(a). If a manufacturer of a herbal product has been granted exclusivity, the FDA will not approve the application and, in most cases, will not even review it unless the second applicant submits a 505(b)(1) application and completes the performance of all the studies required to prove the product's safety and effectiveness. This is true even if the first manufacturer was successful in qualifying the product as a new chemical entity and usage for a specific purpose. Instead of asking the relevant authority for permission to market a product that is not listed in the existing OTC medicine monograph, a manufacturer of herbal drugs after demonstrating the product's efficacy and safety, he should submit an NDA to obtain the necessary regulatory approval to change a monograph.

European Regulations and Guidelines [17, 18]

According to European Directive 2001/83/EC, the efficacy, safety, quality, results of specific tests, and experimental findings are taken into consideration when granting marketing permission for herbal medicinal goods. The Directive 2001/83/EC outlines definitions for traditional herbal medicine, a list of common herbal ingredients, herbal product monographs, and requirements for a streamlined registration process.

The Committee on Herbal Medicinal Products (HMPC), a division of EMA, was established in accordance with Regulation (EC) No 726/2004 and European Directive 2004/24/EC (2004, Sep). The majority of herbal product manufacturers encountered numerous challenges when attempting to comply with European Directive 2004/24/EC's simplification of the registration process while also meeting the standards of Directive 2001/83/EC for efficacy in particular.

The European Pharmacopoeia's HMPC Monographs specify the qualities that must be met by herbal products and pharmaceuticals. Numerous efficacy, safety, quality, non-

clinical, and clinical issues are covered in HMPC guidance materials. Priority herbal constituents, combinations, and products must be identified by HMPC and entered in a monograph.

Community monographs can be used in one of two ways: traditionally (simplified registration) or with well-established use (marketing authorisation). This well while the conventional use segment is developed based on appropriate safety data and the established use segment, which refers to efficacy and safety data likely effectiveness. A community herbal monograph was created by HMPC as a prerequisite for well-established use, marketing permission, traditional use, and scientific registration of herbal medicines based on safety and efficacy evidence of herbal compounds. The Community's non-clinical and clinical data, along with any scientific evaluations of the long-term usage and experience of herbal products, will be documented by HMPC. The majority of herbal medicines receive separate marketing authorization from each of the European Union's member states, although the details surrounding the directive 2004/24/EC unifies the approval of herbal products within the European Union.

The Traditional Herbal Directive 2004/24/EC, which offers a streamlined regulatory clearance process for herbal medicinal goods, was approved by the European Parliament and Council on March 31, 2004.

Recent Developments in Regulations of Herbal Medicines across the World [19, 20, 21]

Global herbal medicine rules have seen significant changes in the twenty-first century, with significant regional and international effects. By determining the efficacy profile and enforcing standards for quality and safety, unpleasant advertising of the indigenous people's traditional herbal remedies that are grown in particular regions is avoided.

The Australian National Medicines Policy governs the use of herbal medicine in Australia.

The policy divides herbal medications into three categories: Registered, Listed, and Exempted. The Australian Therapeutic Goods Administration evaluates the components and preparations based on the first two categories; production should be carried out in accordance with GMP guidelines. The third classification focuses on the limitation to homoeopathic medicines, raw materials and preliminary materials for conditional use, medications with a clear therapeutic application prescribed by the healthcare provider, and medications for personal use [22]. The labelling of herbal medications should adhere to legislation, recognise the seven active ingredients, and indicate the products' intended use, licencing information, state registration information, production processes, and logistics herbal products being imported, selling and advertising regulations, quality control and standardisation, research and development, and animal and human testing. Natural and Non-prescription Health Products Directorate (NNHPD).

Natural Health Products in 2004 published the most recent Canadian rules. To be sold on the Canadian market, National Health Products must obtain a manufacturing licence, an accompanying licence, and an exclusive 8-digit Natural Product Number.

Scope for Harmonization [23, 24]

Pharmacopoeias have outlined guidelines and monographs for herbal medicines. The lack of uniformity in herbal medicine legislation, however, is a big worry for producers of such products because it prevents them from creating standardised goods for the international market. Additionally, many nations have established rules concerning herbal pharmaceuticals. And if that weren't bad enough, different nations have different GMP requirements. Pharmacopoeial standards differ in terms of acceptance criteria, limitations for heavy metals, microbiological contamination, and pesticide limits, which makes it difficult for herbal medical products to comply with the standards of each unique nation.

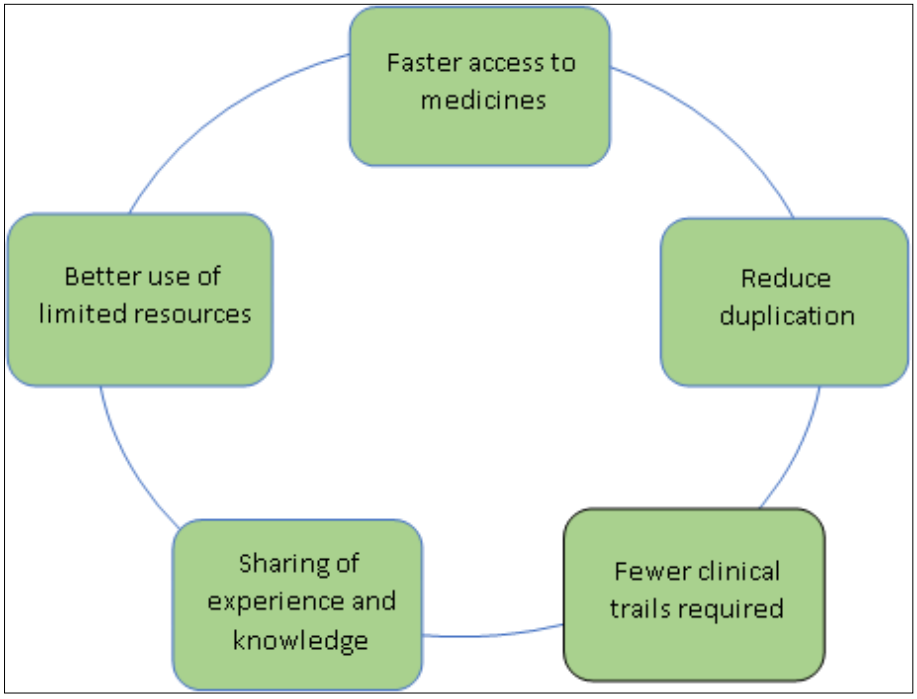

Fig 1: why to promote harmonization?

Harmonization of laws governing herbal medicines will make it possible to manufacture standardised herbal products internationally without facing legal obstacles. Adherence to the GACP, GMP, GLP, and GCP will provide a safe and uniform product because such harmonisation will take time.

Good Agricultural and Collection Procedures (GACP) [25]

The GACP guidelines provide guidance on the cultivation and collection processes, starting with the selection of the herbs, their identification, the characteristics of the soil, the use of appropriate seeds, cultivation techniques, the surroundings and environment, the climatic conditions, the factors to be maintained, and the methods to be employed for harvest. Only trained workers with thorough knowledge of farming methods, pesticide application, etc., should be involved in the collection process. The location where the procedures are carried out needs to be certified for cleanliness, proper aeration, well-oiled equipment, and operational readiness. Pesticide and fertiliser applicators should be less or completely free of contamination, and machines should be calibrated. There should be documentation of all processes, procedures, labelling, agreements, fumigants, and audit findings. After harvesting, methods should be examined acted upon. Herbs should be processed in the designated facilities, and storing should be done properly.

A list of impurities, including the use of fumigants and pesticides, standardisation techniques, and the management of microbial contamination, should be included in the post-testing details. These details should also include information on the use of solvents, stages of purification, and standardisation procedures. It is important to offer accurate data on stability studies.

Good Manufacturing Practices (GMP) [26, 27, 28]

Implementing GMP standards guarantees batch-to-batch product uniformity and adherence to quality standards to satisfy regulatory requirements. A facility that complies with US FDA, EU, or WHO GMP regulations is required since documentation and an effective quality assurance system are essential for GMP. It is essential to establish an R&D lab that adheres to GACP guidelines as well as GLP criteria. A facility would be eligible for the standardised manufacturing of herbal medicines if it meets all of these requirements. From seed-related aspects through the final phases of placement on the shelf, the process of standardisation should be in place with well planned development and validation of analytical test methods.

A thorough product development report for herbal products that includes process controls and a clearly defined process flow will guarantee that quality is built into herbal therapeutic products. A flow chart for manufacturing, coupled with a specification for process control and standard testing protocols, are required for the processing of herbs, herbal products, and herbal preparations. The active plant definition should include physico-chemical characteristics. Contaminants such as pesticides, radioactive materials, toxic and heavy metals, fumigants, fertilisers, adulterants, and unreported chemical substances are examples of impurities that need to be addressed.

Limits for residual solvents should be stated because herbal preparation includes the use of solvent extraction procedures. It is important to provide information on issues relating to the stability of herbal ingredients, herbal preparations, and the herbal product. Information in this area is necessary since the container closing system is a part of the maintenance of quality-related features.

Good Laboratory Practice (GLP) [29]

Analytical technique development and validation at accredited laboratories should be carefully planned in order to assure reproducibility, uniformity, dependability, and consistency of the testing parameters in line with GLP requirements.

Good Clinical Practice (GCP) [30, 31, 32]

Herbals are categorised according to their therapeutic action and nomenclature under the HATC system (Herbal Anatomical Therapeutic Chemical), which supports clinical investigations and safety. A working unit of WHO will be "HATC" under the preview of the "Uppsala monitoring centre". The ATC of Herbals' index and classification guidelines, along with their codes, will be published by HATC.

The Department of AYUSH created a pharmacovigilance programme in 2008 after taking into account the growing adoption of Ayurveda, the significance of maintaining safety and efficacy when using herbal medicines, and the need for attention to report adverse effects and their examination. Adulterants and variations in the herbal nomenclature system are two topics that Uppsala Monitoring (Centre for International Drug Monitoring) handles in relation to herbal pharmacovigilance. By 2011, the Uppsala Monitoring Centre had collected in one database 21,000 complaints of adverse medication reactions related to herbals from 100 different countries.

The Health Authority and Ethical committee give approval for conducting a clinical experiment. Pharmacopoeias, literature, and monographs provide enough information about usage and medical conditions in the nation. When a disease is both acute and chronic, a controlled trial should be conducted. This type of study needs a main investigator and a protocol with thorough documentation of the effectiveness and safety of the herbal medicine.

Standardization of Herbal Medicine Regulations [33, 34, 35]

According to the American Herbal Product association, standardisation is the body of knowledge and the system of checks and balances required to manufacture products with a decent level of consistency. The assurance of the effectiveness, quality, and safety of herbal medicinal products has become a crucial concern as the commercialization of herbal medicine increases. The identification of the herbal plant, fluctuations in seasonal cycles, genotype, chemotype, and ecotype, the presence of xenobiotics, and storage conditions are just a few examples of the variables that might affect the raw material of herbal therapeutic products. By decreasing natural product compositional differences that are already present through the use of QA practises in farming and manufacturing processes, this variation can be prevented. Authentic sample identification and organoleptic evaluation should be taken into account when standardisation techniques are used qualities, phytochemical and pharmacognostic features, volatile natural components, quantitative characteristics such ash values and extraction values, the presence of xenobiotics, tests for microbial load, and toxicity.

Table 1: Reading comparison of herbal medicine (hm) definition and regulation pathways in the drug regulatory authority systems of the uk, germany, usa, united arab emirates (uae), and the kingdom of bahrain

Regulatory Authority	USA	UK	Germany	UAE	Kingdom of Bahrain
Definitions	Botanical preparations are made of plant components, such as Plant substances, algae, microscopic fungus, or a mixture of these substances. Botanical preparations frequently have distinctive qualities, such as complex combinations, a lack of a clear active ingredient, and extensive prior human use.	If a product's active ingredients are herbal, it qualifies as a herbal medication. Only chemicals and/or herbal preparations The processed herbal material may be reduced or powdered, or it may take the form of a tincture, extract, essential oil, expressed juice, or processed exudate. Herbal substances are subjected to specialised methods, such as extraction, distillation, expression, fractionation, purification, concentration, and fermentation to create a herbal product.	Herbal products are medications that are only contain one or more herbal substances, one or more herbal preparations, or one or more of these herbal substances combined with one or more of these herbal preparations as active ingredients. The majority of herbal substances are entire, chopped, or fragmented plants, plant parts, algae, fungi, or lichen that have not been processed and are typically dried, but can occasionally be fresh.	A final product with plant origins is one. When used as directed for prophylactic, therapeutic, or other human health benefits, a labelled medicinal product with aerial or underground plant parts, other plant materials, or combinations thereof, as active ingredients is known as a plant preparation.	The active ingredients in herbal products are herbal. ingredients or herbal remedies, both separately and together "„A herbal substance is an unprocessed, typically dried but occasionally fresh, entire, broken, or cut plant, plant component, algae, fungus, or lichen.
Registration pathways	Dietary supplement under the 1994 DSHEA (which is not registered) or herbal medicine under the Federal Food, Drug, and Cosmetic Act	THR (traditional use) with Directive 2004/24/EC or MA (Traditional) Using Directive 2001/83/EC	Directive 2004/24/EC or MA with THR (traditional use) in accordance with Directive 2001/83/EC	HM with a Ministerial decree or THM (traditional use) No. 3276/1997 for the registration and re-registration of natural source products	With regulatory modifications, a health product (traditional use) law no. (20) of 2015 or medicine containing a vegetable substance with a decision by law no. (18) of 1997
Evidence of quality	Not necessary for dietary supplements GMP standards and QC checks for herbal medications	GMP specifications and QC checks for THR and MA	GMP specifications and QC checks for THR and MA	GMP requirements and quality control checks for conventional HMs and HMs Declaration of Contents Free of Pork Statement of alcohol content	Health product quality checks and GMP requirements and pharmaceuticals containing a vegetable component. Contents declared to be free of pork Alcohol content disclosure
Evidence of safety	Not necessary unless it is an NDI for dietary supplements toxicological evaluations of herbal medications	Bibliographic information for THR Toxicological examinations for MA	Bibliographic information for THR Toxicological examinations for MA	References for conventional HMs Toxicological research on HMs	bibliographic information about pharmaceuticals Toxicological studies on medications including a vegetable substance
	Not necessary for dietary	A lengthy history of use	a lengthy history of use	copies of two conventional	Copies of scholarly work
Evidence of efficacy	Supplements clinical trials for herbal medicines	dating back at least 30 years (including 15 years in the EU) for MA clinical trials with THR	dating back at least 30 years (including 15 years in the EU) for MA clinical trials with THR	HMs or more for each herbal component used in conventional HMs studies in medicine on HMs	that has been published or international health product monographs clinical trials for pharmaceuticals containing a vegetable ingredient
Label requirement	A disclaimer for dietary supplements is required to be included. "The FDA has not reviewed this statement." This product is not meant to be used in the diagnosis, treatment, or prevention of any disease. It must be specified as a dietary supplement on the label.	For THR: a declaration stating that the product is solely depending on history of use A certification mark (THR) is required.	The phrase "traditional medicines" is required for THR. and “typically employed"	No requirements	No requirements

Conclusion and recommendations

Herbal medicine has been a significant part of preserving peoples' health since prehistoric times. Ayurveda and other Indian traditional medical systems, including Unani and Siddha, have a strong scientific foundation for their efficacy, according to recent studies.

The WHO has created manuals for quality control and guidelines for GACP and GCP for medicinal plants and materials. It outlined specific objectives for the effective application of herbal medicine to enhance societal health and healthcare. The WHO has established GMP guidelines to evaluate the purity and security of herbal products in terms of pollutants and residue. Following the appropriate laws and regulations and creating the necessary rules for the delivery of safe goods and its use is reliant on norms, laws, and protocols, which drives global harmonisation forward and boosts the herbal market's expansion to new heights. By establishing good practises with the aid of harmonised standards and herbal monographs, which in the future become a standardised product and enter the market, it is possible to address the issues that herbals face in the areas of safety, quality, and efficacy.

Manufacturers of herbal medical products will be able to create a standardised product for the worldwide market after the regulations have been harmonised.

Acknowledgement

Firstly, I would like to express my sincere gratitude to my respected guide to Principal of Delonix Society's Baramati College of Pharmacy Barhanpur Baramati Dr.Rajendra Patil sir, Dr. Dhananjay Ghodke sir and Assistant professor Miss. Amrata Mantri (M.PHARM) for the continuous support to complete my project work of subject (scope of harmonization of herbal medicine regulations) for his patience, motivation, enthusiasm and immense knowledge. His valuable information helped me a lot to complete my project work. I would not have imagine having a better advisor and mentor for my this study. Last but not least I would like to thanks my family, my parents and my friends for supporting me and spirituality throughout my life.

Reference

1. Ramadoss MSK, Koumaravelou K. Regulatory compliance on herbal medicines-A review, 2019.
2. Yuan H, Ma Q, Ye L and Piao G: The Traditional Medicine and Modern Medicine from Natural Products. Molecules,2016:21:559-59.
3. Wachtel-Galor S, Benzie I. Herbal medicine: an introduction to its history, usage, regulation, current trends, and research needs. Herbal Medicine: Biomolecular and Clinical Aspects,2011L2:234-66.
4. Chaudhary A, Singh N. Contribution of world health organization in the global acceptance of Ayurveda; Journal of Ayurveda and Integrative Medicine, 2011, 2.
5. Wiesner J, Knöss W. Future visions for traditional and herbal medicinal Products - A global practice for evaluation and regulation; Journal of Ethnopharmacology,2014:158:516-18.
6. Sen S, Chakraborty R. Revival, modernization and integration of Indian traditional herbal medicine in clinical practice: Importance, challenges and future; journal of Traditional and Complementary Medicine, 2016.
7. Joshi K: Indian herbal sector 2008.
8. Anonymous: AYUSH, About the System, 2015.
9. World Health Organization: National Policy on Traditional Medicine and Regulation of Herbal Medicinese Report of a WHO Global Survey. Geneva: WHO 2005.
10. Sharma SK, Katoch DC. Current Status & Infrastructure of Ayurveda, 2006.
11. Budhwar V, Yadav S, Choudhary M and Nitesh: A comprehension study on regulation of herbal drugs in USA, European Union and India, 2017.
12. Dietary Supplements: A Framework for Evaluating Safety. Washington, DC: National Academies Press, 2005.
13. Harkey MR, Henderson GL, Gershwin ME, Stern JS and Hackman RM: Variability in commercial ginseng products: an analysis of 25 preparations. Am J Clin Nutr,2001:73:1101-6.
14. Bent S. Herbal Medicine in the United States: Review of Efficacy, Safety, and Regulation. Journal of General Internal Medicine,2010:25(6):854-9.
15. Wu KM, Dou J, Ghantous H, Chen S, Bigger A and Birnkrant D: Current regulatory perspectives on genotoxicity testing for botanical drug product development in the USA. Regulatory Toxicology and Pharmacology,2010:56(1):1-3.
16. Evans S. Changing the knowledge base in western herbal medicine. Social Science & Med,2008:67(12): 2098-2106.
17. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the community code relating to medicinal products for human use, 2001.
18. Enioutina EY, Salis ER, Job KM, Gubarev MI, Krepkova LV, Sherwin CMT. Herbal Medicines: Challenges in the Modern World. Part 5. Status and current directions of complementary and alternative herbal medicine worldwide, 2017.
19. Teng L, Zu Q, Li G, Yu T, Job KM, Yang X, *et al*. Herbal medicines: challenges in the modern world. Part 3. China and Japan. Expert Rev Clin Pharmacol,2016:9:1225-33.
20. Job KM, Kiang TK, Constance JE, Sherwin CM and Enioutina EY: Herbal medicines: challenges in the modern world. Part 4. Canada and United States. Expert Rev Clin Pharmacol, 2016, 1-13.
21. Barnes J, McLachlan AJ, Sherwin CM, Enioutina EY. Herbal medicines: challenges in the modern world. Part 1. Australia and New Zealand. Expert Rev Clin Pharmacol,2016:9:905-15.
22. Sammons HM, Gubarev MI, Krepkova LV, Bortnikova VV, Corrick F, Job KM, *et al.* Herbal medicines: challenges in the modern world. Part 2. European Union and Russia. Expert Rev Clin Pharmacol,2016:9:1117-27.
23. Sahoo N, Manchikanti P. Herbal drug regulation and Commercialization: An Indian industry perspective; The Journal of Alternative and Complementary Medicine,2013:19:957-63.
24. World Health Organization; WHO guidelines on Good Manufacturing Practices on herbal medicines. Geneva: World Health Organization, 2007.
25. Bansal G, Suthar N, Kaur J, Jain A. Stability Testing of Herbal Drugs: Challenges, Regulatory Compliance and Perspectives; Phytotherapy Research,2016:30:1046-58.

26. Mukherjee PK. Problems and Prospects for Good Manufacturing Practice for Herbal Drugs in Indian Systems of Medicine; Drug Information Journal,2002:36:635-44.
27. Kosalec I, Cvek J, Tomić S. Contaminants of Medicinal Herbs and Herbal Products; Archives of Industrial Hygiene and Toxicology,2019:60:485-501.
28. Tandon N and Yadav SS: Contributions of Indian Council of Medical Research ICMR in the area of Medicinal plants/Traditional medicine; Journal of Ethno-Pharmacology,2017:197:39-45.
29. OECD: Principles on Good Laboratory Practice 1998.
30. Drug Statistics Methodology; Guidelines for ATC classification and DDD assignment 2013. WHO Collaborating Centre for Drug Statistics Methodology 2012.
31. Parveen A, Parveen B, Parveen R, Ahmad S. Challenges and guidelines for clinical trial of herbal drugs; Journal of Pharmacy and Bioallied Sciences, 2015, 7.
32. Chugh NA, Bali S, Koul A. Integration of botanicals in contemporary medicine: road blocks, checkpoints and go-ahead signals; Integrative Medicine Research,2018:7:109-25.
33. Nikam PH, Kareparamban J, Jadhav A, Kadam V. Future Trends in Standardization of Herbal Drugs 2012. 7324/JAPS.2012.2631.
34. Bodhisattwa Maiti1, º B.P.2, Rambir Singh1, Pragati Kumar1 and Nishant UpaUpadhyay1: Recent trends in herbal drug.
35. Anquez-Traxler C. The legal and regulatory framework of herbal medicinal products in the European Union: a focus on the traditional herbal medicines category. *Drug Inf. J*,2011:45:15–23. 10.1177/009286151104500102 [CrossRef] [Google Scholar]
36. Alexander J. Qci entrusts 2 agencies as certification bodies for units making ayush products. Pharmabiz, 2010.
37. Verma N. Herbal medicines: Regulation and practice in Europe, United States and India. Int J Herb Med,2013:1(4):1-5.