

Phytopharmaceutical Application and Recent Advances: A Review

¹Ms. Neha S. Gallani, ²Dr. Sachin J. Dighade, ³Bhushan P. Deshmukh

¹Lecturer, Institute of Pharmacy and Research Anjangaon Bari Road, Badnera Amravati 444701

²Principal, Institute of Pharmacy and Research Anjangaon Bari Road, Badnera Amravati 444701

³Student, Institute of Pharmacy and Research Anjangaon Bari Road, Badnera Amravati 444701

Submitted: 01-03-2022

Accepted: 13-03-2022

ABSTRACT: A Phytopharmaceutical is a complex mixture derived from plant sources that is used as a medicine or drug. The Ministry of Health has begun the standardization of the names of all Phytopharmaceutical preparations. The development of Phytopharmaceutical products, which might partially substitute some of the conventional medications demanding imported raw materials, and which could be produced by pharmaceutical industries based in developing countries through joint projects. Highest demands are made on clinically proven phyto-pharmaceuticals. Their effect and safety have to be verified in randomized, double-blind, (placebo)-controlled clinical trials. They are developed and scientifically evaluated in the same way as conventional medicinal products. Globally, herbal medicine has been considered an important alternative to modern allopathic medicine. While they have become very popular, only selected herbs have been scientifically evaluated for their potential in medical treatment. The new drug Vereen (Polyphenol E) Ointment is the first prescription botanical (herbal) drug approved by the U.S. FDA under the "new" drug amendments of 1962 that required drugs to be proven safe and effective prior to being marketed in the U.S. Because of the unique health benefits and relatively low side effects, natural products such as food/dietary supplements, nutraceuticals and herbal medicines have been gaining popularity all over the world the gap between the popularity of these remedies and the frequently weak scientific basis of their use is striking. In reality, the efficacy and true frequency of side effects for most herbal medicine products is not known because the majority have not yet been tested in large clinical trials and because pharmacovigilance systems are much less extensive than those in place for pharmaceutical products. In contrast to the popularity of herbal medicinal products, physicians and consumers often have a very critical view of robust efficacy and safety

profiles. Application of pharmaceutical nanotechnology for plant actives and extracts, is gaining a tremendous growth and interest among the scientist.

KEYWORDS:

Phytopharmaceutical, Classification of Phytopharmaceutical, Traditional system of medicine, Phytopharmaceutical Application, Recent Advances

I. INTRODUCTION

Phytopharmaceutical: -Phytopharmaceutical drug is defined as purified and standardized fraction with defined minimum four bio-active or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation, or prevention of any disease or disorder but does not include administration by parenteral route. Globally, herbal medicine has been considered an important alternative to modern allopathic medicine. Although the herbal medicines are very popular in the society, only few medicinal herbs have been scientifically evaluated for their potential in medical treatment. In most countries, the herbal drugs are poorly regulated and are often neither registered nor controlled by the health authorities. [1]

II. CLASSIFICATION OF PHYTOPHARMACEUTICAL:-

2.1 Definitions

A. Herbal drugs: -

Are mainly whole, fragmented or cut, plants, algae, fungi, lichen, in an unprocessed state, usually in dried form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal drugs.

B. Herbal medicinal products: -

Are those medicinal products which, as active substances, solely contain herbal drug preparation, such as comminute parts of plants, extracts, pressed juice or distillates of plants. Isolated plant constituents such as dig toxin or menthol, as well as homeopathic medicinal products, are not regarded as herbal medicinal products.

C. Marker substances: -

Are chemically defined constituents of herbal drugs, herbal drug preparations and herbal medicinal products which, according to the state of scientific knowledge, do not contribute to the therapeutic activity else only serve analytical purposes.

D. Drug: -

as per Section 3(b) of D and C act 1940 "Drug" includes all medicines for internal or external use of human beings or animals and all substances intended to be used for or in the diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, Including preparations applied on human body for the purpose of repelling insects like mosquitoes.

E. Traditional medicine: -

Is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.

F. Ayurveda, siddha, unani drugs:-

include all medicines intended for internal or external use for or in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals and manufactured exclusively in accordance with the formulae described in, the authoritative books of Ayurveda, Siddha and Unani Tibb system Of medicine, specified in the First Schedule

G. Patent or proprietary medicine: -

in relation to Ayurvedic, Siddha or Unani Tibb systems of medicine of all formulations containing only such ingredients mentioned in the formulae described in the authoritative books of Ayurveda, Siddha or Unani Tibb system of medicine specified in the first Schedule but does not

include a medicine which is administered by parenteral route and also a formulation included in the authoritative books as specified in clause (a).

H. Phytopharmaceutical drugs:-

as per D and C act 1940, these include purified and standardized fraction with defined minimum four bioactive or phytochemical compounds (qualitatively and quantitatively assessed) of an extract of a medicinal plant or its part, for internal or external use of human beings or animals for diagnosis, treatment, mitigation or prevention of any disease or disorder but does not include administration by parenteral route. As per gazette notification dated 24th October, 2013, "Phytopharmaceutical drug" includes processed or unprocessed standardized materials derived from plants or parts thereof or combination of parts of plants, extracts or fractions thereof in a dosage form for internal or external use of human beings or animals and intended to be used for diagnosis, treatment, mitigation or prevention of any disease or disorder in human beings or animals, but does not include administration by parenteral route".

I. New Phytopharmaceutical drug:-

As defined in the Act including bulk drug substance which has not been used in the country to any significant extent under the conditions prescribed, recommended or suggested in the labelling thereof and has not been recognized as effective and safe by the licensing authority mentioned under rule 21 for the proposed claims: Clinical trial (Clinical study) is a systematic study of ASU drug/ Patent or Proprietary Medicines on human subjects-(whether patients or non-patient volunteers)-in order to discover or verify the clinical, pharmacological (including pharmacodynamics/ pharmacokinetics), and/or adverse effects, with the object of determining their safety and/or efficacy.

2.2 Indian system of medicine (ISM)

The Indian System of Medicine is of great antiquity. It is the culmination of Indian thought of medicine which represents a way of healthy living valued with a long and unique cultural history, as also amalgamating the best of influences that came in from contact with other civilizations be it Greece (resulting in Unani Medicine) or Germany (Homeopathy) or our scriptures/sages which gave us the science of Ayurveda, Siddha as also Yoga and Naturopathy. Like the multifaceted culture in our country, traditional medicines have evolved over

centuries blessed with a plethora of traditional medicines and practices. [2]

1) **Ayurveda (900-800 BC)**



Figure No.1:- Ayurveda Medicine

Ayurveda is the oldest traditional medicinal systems of India that is meant for preventive, promotive and curative healthcare originating from the Vedas. 'Ayu', i.e. life and 'Veda', i.e. knowledge constitute the word 'Ayurveda'. Ayurveda is an alternative medicine system with historical roots in the Indian subcontinent. [3]

2) **Siddha (800-700 BC)**



Figure No.2:- Siddha Medicine

The Siddha System of medicine is one of the ancient systems of medicine in India having its close bed with Dravidian culture. The term Siddha means achievements and Siddhars are those who have achieved perfection in medicine. [4]

3) **Unani (460-377 BC)**



Figure No.3:- Unani Medicine

Unani system of medicine is a comprehensive medical system, which provides preventive, promotive, curative and rehabilitative health care. The system is holistic in nature and takes into account the whole personality of an individual rather than taking a reductionist approach towards disease. The fundamentals, diagnosis and treatment modalities of the system are based on scientific principles. [5]

4) **Homeopathy (1850 AD)**



Figure No.4:- Homeopathy Medicine

"Homoeopathy" was introduced as a scientific system of drug therapeutics by a German Physician, Dr. Christian Frederick Samuel Hahnemann in 1805. While translating a medical treatise by Scottish physician and chemist, William Cullen, from English to German, in 1790, he came across a foot note under Cinchona that attributed its fever curing property to the astringent (decongestant) qualities of the drug. [6]

5) **Naturopathy**



Figure No. 5:- Naturopathy

Naturopathy is rooted in the healing wisdom of many cultures and times based on principal of natural healing. The principles and practices of Naturopathy are integrated in the life style, if the people observe living close to nature. Naturopathy is a cost effective drugless, non-invasive therapy involving the use of natural materials for health care and healthy an living. [7]

2.3 Regulation of herbal drugs

Globally, herbal medicine has been considered an important alternative to modern allopathic medicine. Although the herbal medicines are very popular in the society, only few medicinal herbs have been scientifically evaluated for their potential in medical treatment. In most countries, the herbal drugs are poorly regulated and are often neither registered nor controlled by the health authorities.[8]

Acts administered in the ISM sector

- ❖ Central Council of Indian Medicine Act-1973
- ❖ Central Council of Homoeopathy Act-1973
- ❖ Drugs and Cosmetics Act-1940
- ❖ Drugs and Magic Remedies Act-1954, 1955 and Rules there under

2.4 Problems with regulated herbal products

As herbal drugs are not uniformly regulated and are poorly documented, there could be many reasons behind this. Herbal medicines are generally considered as safe. However, herbal drugs are not always safe as they are promoted. The assumption that everything that is natural is safe not correct. This is due to the quality related safety issues and it needs information of primary processing and quality specifications. The following issues are need to be addressed for fully regulated herbal medicines.

- ❖ Quality control
- ❖ Safety of the herbal preparations
- ❖ Development of effective marker
- ❖ Clinical efficacy of marker
- ❖ Documentation
- ❖ Regulatory harmonization

III. PREPARATIONS AND STANDARDIZATION OF AYURVEDIC FORMULATIONS

From traditional period, the herbals, animals & its products, minerals and marine materials including metals are taken as such or in the form of extracts, or in form of formulations. The different types of formulations are powders (bhasma, churna, mandur, parpati, pishti, rasayan and satva), liquids (arishta, arka, asava, drawana, kwath, swaras and taila), semisolids (avaleha, ghrita, kalka and rasayoga) and tablets (gutika, vati and vatika)

3.1 Asavas and Aristas:-

Asavas and Aristas are medicinal preparations made by adding the drugs either in

powder form or as Kasayas with solution of sugar or jaggery for a specified/stipulated period of time. Fermentation that sets in generation of alcohol that facilitates the extracties of the active principle contained in the drug. This self-generated alcohol also serves a preservative. The preparations made using kasaya are called Aristas and the other Asavas.

A. Asavas :-

The required quantity of water is boiled this is poured into an earthen pot and jaggery, sugar, etc. are dissolved. Finally, powdered drugs mentioned in the formula are added, the pot is covered with lid and the edges are sealed with clay-smearred cloth in seven consecutive layers. The rest of the process is as in the case of Arista.

B. Aristas :-

The drugs are coarsely powdered and the Kasaya is prepared. The Kasaya is filtered and kept in an earthen pot. The sugar or jaggery, according to the preparation, is added and dissolved. The drugs indicated as PrakshepanaChurna are finely powdered and added. At the end, Dhataki Pushpa (Woodfordiafruiticosa flowers used as fermentation initiators added. The mouth of the pot is covered with the earthen lid and the edges are sealed with clay smeared cloth in seven consecutive layers.

3.2 Avaleha:-

Avaleha or Lehya is a semisolid preparation of drugs, prepared with the addition of jaggery, sugar-candy or Khandasari and boiled along with a prescribed liquid.

3.3 Churna:-

The Churna is fine powder of a drug. Churna is defined as a fine powder of drug or drugs in Ayurvedic system of medicine. Drugs mentioned in patha, are cleaned properly, dried thoroughly, pulverised and then sieved. The churna is free flowing and retains its potency for one year, if preserved in an airtight containers. . Churna formulation are similar to powder formulations in Allopathic system of medicine.

3.4 Bhasma

Bhasma is that which is burnt to powder. This name is generally applied to all that are subjected to the process of burning and reduction to ash. In this section, it is applied to the metals, minerals and animal products which are, by special processes, calcinated in closed crucibles in pits with cow dung cakes (Putam). Bhasmas are generally,

white pale or red in colour. The colour of preparations mostly depends on the parent material

3.5 Vati and Gutika

Vati and Gutika are presented as tablets or pills. These are made of various drugs, of mineral, animal and vegetable origin. Vati is a preparation where different medicinal substances are used. To make tablets (vati) and pills (gutika). This is done either by cooking the powdered herbs with jaggery or guggulu or without cooking by macerating the powder with any liquid like honey and guggulu and then rolled into pills. [9]

IV. APPLICATION OF PHYTOPHARMACEUTICAL

Phytopharmaceuticals refer to a group of natural substances that include anthocyanin's, carotenoids, lycopene's, flavonoids, glucosinolates, isoflavonoids, limonoids, polyphenols, omega-3 fatty acids, phytoestrogens, resveratrol, phytosterols, probiotics and terpenoids with specific pharmacological effects in human body. Some of them are summarized below:-

i. Carotenoids:-

The most common examples of carotenoids are α -carotene, β carotene, lycopene, lutein, and zeaxanthin. Some of them such as β -carotene, lycopene, lutein and zeaxanthin have been reported to be in reverse to the risk of cardiovascular diseases, some kinds of cancers and eye disorders. However, lutein has various kinds of therapeutic effects and protects against uterine, prostate, breast, colorectal and lung cancers. It also protects gastrointestinal cancer. Carotenoids have antioxidant properties by which they show their beneficial effects. [10]

ii Lycopene:-

It is class of carotenoids but deficient in pro-vitamin A activity. It is present in various fruits and vegetables. Intake of lycopene rich dietary food items like tomatoes and products thereof is associated with lowering in the chance of chronic disorders like cancer and cardiovascular diseases. Increase in serum and tissue lycopene levels decreases the risk of various chronic diseases [11]

iii Flavonoids:-

Flavonoids are polyphenolic compounds which are usually obtained in fruits and vegetables like berries, legumes, tea, grapes, olive oil, cocoa, walnuts, peanuts, spices, fruits, and green

vegetables, onion, apple, berries and tea. These are reported to be active against various bacterial disease, oxidation, viral diseases and algesia. Bunch of flavonoids are the plant phenols and ketones such as flavanones, dihydroflavonols, flavones and flavanols. [12]

iv Limonoids:-

Limonoids are present in citrus fruits as major source of terpenoids. These are highly oxygenated tri-terpenoids with substantial anticancer actions. D-limonene is the commonest monocyclic monoterpene, found in orange peel oil and inhibits pancreatic cancer. [13]

v Terpenoids:-

These are also known as isoprenoids. These are the largest class of phyto-nutrients in green foods and grains. These are obtained from mosses, liverworts, algae and lichens, as well as in insects, microbes or marine organisms. These are required to fix carbon through photosynthetic reactions using photosensitizing pigments. Animals have evolved to utilize these compounds for hormonal and growth regulatory functions. The presence of these molecules in animal tissues also provides a measure of protection from certain diseases. [14]

vi Omega-3 fatty acids:-

There is extensive interest in increasing consumption of omega-3 fatty acids because they are associated with many health benefits. The main food sources of the long chain omega-3 fatty acids are fish, especially fatty species such as salmon, rainbow trout, mackerel, herring and sardines. Some plants, mainly canola, soybean and flax oils provide the 18-carbon omega-3 fatty acid, alpha-linolenic acid. The benefit of omega-3 fatty acids in the treatment of people suffering from osteoarthritis is well known. In people who have osteoarthritis, increased consumption of omega-3 fatty acids and adequate intake of monounsaturated fatty acids such as those found in olive oil (and reduced consumption of omega-6 fatty acids) can improve symptoms and even sometimes allow a reduction in the use of nonsteroidal anti-inflammatory drugs (NSAIDs). [15]

vii Phytoestrogens:-

Phytoestrogens are non-steroidal phytochemicals quite similar in structure and function to gonadal estrogen hormone. They offer an attractive alternate for hormone replacement therapy (HRT) with beneficial effects on

cardiovascular system and may even alleviate menopausal symptoms. They are potential alternatives to the synthetic selective estrogen receptor modulators, which are currently applied in HRT. On the basis of chemical structure, phytoestrogens can be classified as flavonoids, isoflavonoids, coumestans, and stilbenes. [16]

viii Resveratrol:-

It is a natural phytoalexin which is made by the plants in stress conditions and pathogen attack. It is produced after various physiological effects. At lower dose which is normally intake by food, resveratrol has been reported to exert neuroprotective and cardioprotective effects. This is due to its antioxidant properties. It is recognized for its widespread therapeutic actions like antithrombogenic, anti-inflammatory, and cardioprotective, neuroprotective, antiageing and anticancer. Resveratrol is found in considerable concentrations in grapes, peanuts, etc. [17]

ix Phytosterols:-

These are defined as plant sterols and plant stanols. Phytosterols lower total and blood cholesterol level by preventing cholesterol absorption from the intestine. Phytosterols are naturally found in fruits, vegetables, nuts and principally oils. Market demand for phytosterol-fortified products is expected to increase in near future as the growth rate of cardiovascular disease is being increased in India. There is no doubt that phytosterols a functional food ingredient will be a new approach to reduce cholesterol level and hold a great promise for long term health management. [18]

V. PHYTOPHARMACEUTICAL RECENT ADVANCES

5.1 Advances in the standardization of herbal drugs

I. Standardization of herbal formulation :-

Standardization of herbal formulation requires implementation of Good Manufacturing Practices (GMP) In addition, study of various parameters such as pharmacodynamics, pharmacokinetics, dosage, stability, self-life, toxicity evaluation, chemical profiling of the herbal formulations is considered essential"[19] Other factors such as pesticides residue, aflatoxine content, heavy metals contamination, Good Agricultural Practices (GAP) in herbal drug standardization are equally important"[20]

II Conventional methods for standardization of herbal formulation

Standardization of herbal raw drugs include passport data of raw plant drugs, botanical authentication, microscopic & molecular examination, identification of chemical composition by various chromatographic techniques and biological activity of the whole plant. [21] Macroscopic and microscopic evaluation and chemical profiling of the herbal materials for quality control and standardization have been reported by various workers' " Macroscopic identity of medicinal plant materials is based on sensory evaluation parameters like shape, size, colour, texture, odour and taste while microscopy involves comparative microscopic inspection of powdered herbal drug.[22]

III Herbal drug standardization:-

Standardization is a system that ensures a predefined amount of quantity, quality & therapeutic effect of ingredients in each dose".[23] Herbal product cannot be considered Scientifically valid if the drug tested has not been authenticated and characterized in order to ensure reproducibility in the manufacturing of the product Moreover, many dangerous and lethal side effects have recently been reported, including direct toxic effects, allergic reactions, effects from contaminants, and interactions with herbal drugs". Therapeutic activity of an herbal formulation depends on its phytochemical constituents. [24]

IV Standardization of polyherbal formulations:-

Standardization is an important aspect for maintaining and assessing the quality and safety of the polyherbal formulation as these are combinations of more than one herb to attain the desired therapeutic effect".[25]The polyherbal formulation of hyperlipidemia has been standardized on the basis of organoleptic properties, physical characteristics, and physico-chemical properties The formulation and standardized of a polyherbal formulation (Artrex®) designed for the treatment of arthritis containing four botanicals was carried out using modern scientific tools and with known markers, has been granted a US patent.[26]

V ISSR (Inter-Simple Sequence Repeat)

ISSR, a PCR-based application is unique and inexpensive popular technique of DNA fingerprinting which include the characterization of genetic fingerprinting, gene tagging, detection of clonal variation, phylogenetic analysis, detection of

genomic instability, and assessment of hybridization".[27]

5.2 Recent approaches in herbal drug standardization:-

a) DNA fingerprinting

Correct identification and quality assurance of the starting material is an essential prerequisite in herbal medicine to ensure reproducible quality of herbal medicine, which contributes to its safety and efficacy (Joshi et al., 2004; Straus, 2002; De Smet, 2002). DNA analysis has been proved as an important tool in herbal drug standardization. This technique is useful for the identification of phytochemically indistinguishable genuine drug from substituted or adulterated drug. It has been reported that DNA fingerprint genome remain the same irrespective of the plant part used while the phytochemical content will vary with the plant part used, physiology and environment.

b) Methods of identification and emerging techniques

Most of the regulatory guidelines and pharmacopoeias suggest macroscopic and microscopic evaluation and chemical profiling of the botanical materials for quality control and standardization (WHO, 1998; Indian Herbal Pharmacopoeia, 2002; British Herbal Pharmacopoeia, 1996). Chemical profiling establishes a characteristic chemical pattern for a plant material, its fractions or extracts. Thin layer chromatography (TLC) and high performance thin layer chromatography (HPTLC) are routinely used as valuable tools for qualitative determination of small amounts of impurities.

c) Chromatographic fingerprinting

Chromatographic fingerprinting has been in use for a long time for single chemical entity drug substances. Recently it has become one of the most powerful approaches to quality control of herbal medicines. The use of chromatographic fingerprinting for herbal drugs tends to focus on identification and assessment of the stability of the chemical constituents observed by chromatography. Chemical and chromatographic techniques may also be used to aid in identification of an herbal material or extract. Where active ingredients contributing to therapeutic efficacy are known, botanical preparations should be standardized to these compounds a marker substance which should be specific for the botanical could be chosen for

analytical purposes, although it should only serve for internal batch control. [28]

5.3 Recent Advances in the Chemical, Manufacturing and Regulatory Aspects of Phytopharmaceutical

A. Chemistry and Analysis

Black radish yield several Phytopharmaceutical Ginkgolic acids is found in leaf extracts and Phytopharmaceutical from Ginkgo biloba Linn. Flavonoids have determined to be active in Ginkgo biloba L. and its Phytopharmaceutical. These flavonoids include epicatechin, catechin, rutin, apigenin, luteolin, and quercetin. Ginkgolides and bilobalide are estimated in Phytopharmaceutical using liquid chromatography-mass spectrometry (LC-MS). Frankincense gum also finds utility as Phytopharmaceutical and its triterpenic acids are characterized using HPLC-PDA.[29]. Flavonoids and terpene lactones in Ginkgo biloba L. Phytopharmaceutical have been identified using HPLC.[30] Three flavonols - quercetin, kaempferol, and isorhamnetin – have been identified in Hippophaerhamnoides Phytopharmaceutical by HPLC. Cinchona in Ib has been identified in phytopharmaceuticals of Trichiliacatigua by HPLC. Antioxidants in Nigella sativa L.) Phytopharmaceuticals have been quantified using HPLC. HPLC-DAD has been used for estimating antioxidants and caffeine in phytopharmaceuticals. Metabolic fingerprinting based on MS and NMR has a definite role in the quality control of phytopharmaceuticals. [31]

B. Production and Regulatory Aspects:-

Synergy research in phytopharmaceuticals has also attracted the attention of scientific community DNA barcoding may be used for exact identification of plant species and hence, play an important role in development of better phytopharmaceuticals.[32] Pre-formulation of Ayurvedic phytopharmaceuticals has also been reported. Phytosome are debated to be an efficient formulation of phytopharmaceuticals.[33] Contemporary approaches in phytopharmaceuticals production by use of plant biotechnology have been discussed Biotechnological yield of phytopharmaceuticals has also been a matter of discussion. Pharmaceutical nanotechnology may soon help in expansion of phytopharmaceuticals, herbal extracts and bioactives. Drugs and cosmetics rules in India needed amendment(s) in case of

phytopharmaceuticals. Phytopharmaceuticals are now regulated in India. [34]

VI. CONCLUSION: -

Increasing importance of plant based natural product including extracts, enrich fraction, essential oils, Phyto molecules, flavours and fragrances attracts the pharmaceutical as well as cosmetic industry. The new Phytopharmaceutical regulation encourages and permits the development of plant-based drugs using advanced techniques of solvent extraction, fractionation, potentiating steps, modern formulation development, the combination of qualitative fingerprinting and quantitate multicomponent analysis is a novel and rational method to address the key issues of quality control of herbal medicines.

The advancement of analytical techniques will serve as a rapid and specific tool in the herbal research, thereby, allowing the manufacturers to set quality standards and specifications the applications of high-technology oriented advanced hyphenated techniques will serve as a rapid and unambiguous tool in the Phytopharmaceutical research, thereby, benefiting the entire pharmaceutical industry.

REFERENCE:-

- [1]. Bhatt, A., 2016. Phytopharmaceuticals: A new drug class regulated in India. Perspectives in clinical research, 7(2), p.59.
- [2]. Nooreen, Z., Rai, V.K. and Yadav, N.P., 2018. Phytopharmaceuticals: A new class of drug in India. Ann. Phytomed, 7(1), pp.27-37.
- [3]. Parasuraman, S., Thing, G.S. and Dhanaraj, S.A., 2014. Polyherbal formulation: Concept of ayurveda. Pharmacognosy reviews, 8(16), p.73.
- [4]. Vaidya, A.D. and Devasagayam, T.P., 2007. Current status of herbal drugs in India: an overview. Journal of clinical biochemistry and nutrition, 41(1), pp.1-11.
- [5]. Kalim, M.D., Bhattacharyya, D., Banerjee, A. and Chattopadhyay, S., 2010. Oxidative DNA damage preventive activity and antioxidant potential of plants used in Unani system of medicine. BMC Complementary and alternative medicine, 10(1), pp.1-11.
- [6]. Poitevin, B., 1999. Integrating homoeopathy in health systems. Bulletin of the World Health Organization, 77(2), p.160.
- [7]. Elder, C.R., 2013. Integrating naturopathy: can we move forward?. The Permanente Journal, 17(4), p.80.
- [8]. Bandaranayake, W.M., 2006. Quality control, screening, toxicity, and regulation of herbal drugs. Modern Phytomedicine, 10(9783527609987).
- [9]. Sathya Dr.S, JaiganeshDr.K.P,SudhaDr.T, Herbal Drugs Technology, Pee Vee Publication, Page No 71-95
- [10]. Rashid, S., Majeed, L.R., Nisar, B., Nisar, H., Bhat, A.A. and Ganai, B.A., 2021. Phytomedicines: Diversity, extraction, and conservation strategies. In Phytomedicine (pp. 1-33). Academic Press.
- [11]. Bohn, T., 2019. Carotenoids and markers of oxidative stress in human observational studies and intervention trials: Implications for chronic diseases. Antioxidants, 8(6), p.179.
- [12]. Panche, A.N., Diwan, A.D. and Chandra, S.R., 2016. Flavonoids: an overview. Journal of nutritional science, 5.
- [13]. Suntar, I., Khan, H., Patel, S., Celano, R. and Rastrelli, L., 2018. An overview on Citrus aurantium L.: Its functions as food ingredient and therapeutic agent. Oxidative medicine and cellular longevity, 2018.
- [14]. Singh, B. and Sharma, R.A., 2015. Plant terpenes: defense responses, phylogenetic analysis, regulation and clinical applications. 3 Biotech, 5(2), pp.129-151.
- [15]. Bradberry, J.C. and Hilleman, D.E., 2013. Overview of omega-3 fatty acid therapies. Pharmacy and Therapeutics, 38(11), p.681.
- [16]. Rietjens, I.M., Lousse, J. and Beekmann, K., 2017. The potential health effects of dietary phytoestrogens. British journal of pharmacology, 174(11), pp.1263-1280.
- [17]. Keylor, M.H., Matsuura, B.S. and Stephenson, C.R., 2015. Chemistry and biology of resveratrol-derived natural products. Chemical reviews, 115(17), pp.8976-9027.
- [18]. Lin, Y., Knol, D. and Trautwein, E.A., 2016. Phytosterol oxidation products (POP) in foods with added phytosterols and estimation of their daily intake: A literature review. European Journal of Lipid Science and Technology, 118(10), pp.1423-1438.
- [19]. Mosihuzzaman, M. and Choudhary, M.I., 2008. Protocols on safety, efficacy, standardization, and documentation of herbal medicine (IUPAC Technical Report). Pure

- and Applied Chemistry, 80(10), pp.2195-2230.
- [20]. Bauer, R., 1998. Quality criteria and standardization of phytopharmaceuticals: Can acceptable drug standards be achieved?. *Drug Information Journal: DIJ/Drug Information Association*, 32(1), pp.101-110.
- [21]. Maegawa, H., Nakamura, T. and Saito, K., 2014. Regulation of traditional herbal medicinal products in Japan. *Journal of ethnopharmacology*, 158, pp.511-515.
- [22]. Bhutani, K.K., 2003. Herbal medicines an enigma and challenge to science and directions for new initiatives. *Indian J Nat Prod*, 19(1), pp.3-8.
- [23]. Sagar, B.P., Zafar, R., Panwar, R., Kumar, V. and Mangla, A., 2005. Herbal drugs standardization. *The Indian Pharmacist*, 4(35), pp.19-22.
- [24]. Vaidya, A.D. and Devasagayam, T.P., 2007. Current status of herbal drugs in India: an overview. *Journal of clinical biochemistry and nutrition*, 41(1), pp.1-11.
- [25]. Sharma, A.K., Gaurav, S.S. and Balkrishna, A., 2009. A rapid and simple scheme for the standardization of polyherbal drugs. *International Journal of Green Pharmacy (IJGP)*, 3(2).
- [26]. Patwardhan, B., Patwardhan and Bhushan, 1996. Method of treating musculoskeletal disease and a novel composition therefor. U.S. Patent 5,494,668.
- [27]. Kiran, U., Khan, S., Mirza, K.J., Ram, M. and Abdin, M.Z., 2010. SCAR markers: a potential tool for authentication of herbal drugs. *Fitoterapia*, 81(8), pp.969-976.
- [28]. Yadav, N.P. and Dixit, V.K., 2008. Recent approaches in herbal drug standardization. *Int J Integr Biol*, 2(3), pp.195-203.
- [29]. Büchele, B., Zugmaier, W. and Simmet, T., 2003. Analysis of pentacyclic triterpenic acids from frankincense gum resins and related phytopharmaceuticals by high-performance liquid chromatography. Identification of lupeolic acid, a novel pentacyclic triterpene. *Journal of Chromatography B*, 791(1-2), pp.21-30.
- [30]. Mesbah, M.K., Khalifa, S.I., El-Gindy, A. and Tawfik, K.A., 2005. HPLC determination of certain flavonoids and terpene lactones in selected *Ginkgo biloba* L. phytopharmaceuticals. II *Farmaco*, 60(6-7), pp.583-590.
- [31]. Van Der Kooy, F., Maltese, F., Choi, Y.H., Kim, H.K. and Verpoorte, R., 2009. Quality control of herbal material and phytopharmaceuticals with MS and NMR based metabolic fingerprinting. *Planta medica*, 75(07), pp.763-775.
- [32]. Osathanukul, M., Suwannapoom, C., Osathanukul, K., Madesis, P. and de Boer, H., 2016. Evaluation of DNA barcoding coupled high resolution melting for discrimination of closely related species in phytopharmaceuticals. *Phytomedicine*, 23(2), pp.156-165.
- [33]. Shakeri, A. and Sahebkar, A., 2016. Phytosome: a fatty solution for efficient formulation of phytopharmaceuticals. *Recent Patents on Drug Delivery and Formulation*, 10(1), pp.7-10.
- [34]. Kokate, C., Jalalpure, S.S. and Pramod, H.J., 2011. *Textbook of Pharmaceutical Biotechnology-E-Book*. Elsevier Health Sciences.