Traditional plant-based medications and herbal remedies: health, safety, and quality problems

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Abstract: **Herbal therapies and plant-based medications are regarded as pure, safe, and healthful because they come from Herbal therapies and plant-based medications are regarded as pure, safe, and healthful because they come from natural resources. However, consumers need to know more about the efficacy, safety, and general health of these items given the rising acceptance and usage of herbal remedies and a plant-based traditional therapies.Most medical plant material is collected from wild stocks, where a variety of plant-based chemical elements are produced as a result of both extrinsic and intrinsic conditions.Plant material containing differing amounts of physiologically active chemicals may influence the medication's safety and efficacy. In addition, plants emit secondary metabolites that can repel, poison, or even kill harmful species.**

Therefore, certain physiologically active second-generation metabolites may have genotoxic, mutagenic, or cancer-causing properties.Contaminants from manmade or natural sources frequently degrade the effectiveness of herbal therapies and traditional medications, leading to negative side effects or even death. This essay offers an extensive understanding of the biotic and abiotic elements that could influence the variation in bioactive concentrations.Furthermore, pollutants that could degrade traditional medicine quality and cause unfavorable side effects are examined, and data on poisonings following Significant issues are raised by the usage of traditional medicine.

Keywords: Negative side effects, biologically active substances, contamination poisoning quality, secondary compounds.

INTRODUCTION

The pharmaceutical sector and certain governmental organisations have been cutting back on their support for research into complex NPs, including botanical extracts. However, secondary metabolites continue to be a "muse" for the creation of new medications [1]. Reaffirmed mostly by traditional medical systems like Chinese and Ayurvedic, herbal medicines (HMs) and other items derived from plants remain valuable possibilities for treating a variety of illnesses [2-3]. However, the market for NPs with questionable therapeutic benefits also warrants investigation, particularly in light of the proliferation of medical misinformation on social media [4].These products, regardless of the application, possess a chemically complex makeup that allows them to operate on several targets, resulting in pharmacological and/or toxicological effects[5].Since ancient times human beings have been employing plants and their parts for therapeutic purposes. Concern over using medicinal plants in addition to prescription medications is growing among patients suffering from chronic conditions such as cancer, High blood sugar level, HIV/AIDS and high blood pressure [6-7].Most people believe that medicinal plants are completely safe since they come from nature and so they are combined with conventional drugs[8]. A few further factors contributing to the popularity of medical herbs include their increased accessibility, affordability, efficacy, and patient reports of side effects and unhappiness with traditional treatments, as well as positive prior experiences with using medicinal plants [9-10].This study delves into the use of traditional plant-based medicine and examines how various factors, both biotic and abiotic, can impact the concentrations of bioactive compounds.It also talks about the possible problems that might occur concerning the quality of plant material that is harvested and any adverse effects that might be linked with the administration of plant-based traditional medicines.

ABIOTIC STRESS

One type of environmental condition that restricts plant growth and metabolism is called abiotic stress[11]. Important food and cash crops production and yields are predicted to be reduced by more than 50% due to abiotic stressors[12]. Abiotic stressors fall into two categories: those that occur above ground and those that occur below.Stresses induced by the atmosphere are called atmospheric-induced abiotic stresses, while those produced by soil are termed edaphic.[13]. Abiotic stresses derived from the atmosphere are common in areas with varying climates and patterns of precipitation, which are typified by protracted dry spells broken up by heavy downpours[14]. However, anthropogenic practices like fertilising with sewage sludge, fumigating with inorganic chemicals, and irrigation with brackish and waste water can lead to abiotic stresses of edaphic origin[15].

Table 01: Examples of how abiotic stress conditions affect plants and how they produce secondary metabolites.

Abiotic stress factor	Stress factors' effects on plants and how they produce specialised metabolites
a) Salt	When salt stress occurs, cells lose water and are put under osmotic pressure and ionic stress,which in turn causes plants to either accumulate or reduce secondary metabolites. For instance, plants under salinity stress exhibit a significant rise in anthocyanins; in contrast, anthocyanin concentrations fall in species of plants that are sensitive to salinity. In Lycopersicon esculentum, proline concentrations rise, while polyphenol concentrations are seen to rise in a number of plant species. In contrast, under salt stress, tropane alkaloids rise in Datura innoxia, trigonelline in Glycine max, and flavonoids in Hordeum vulgare[16] Under salt stress, plants increase production of substances including phenols, terpenes such as Amygdalin, alkaloids and glucosinolates that contain N and S[17].
b) Drought	Drought stress is evidently responsible for the accumulation of a lipophilic resins in Larrea & Diplacus particular species, which subsequently assume a UV screen protection role. As a result, phenolic compounds are produced at a higher rate.Furthermore, there is a link among xylem pressure & tannin production that, depending on the degree of drought stress encountered, might be positive or negative[18].When plants experience oxidative stress, their redox homoeostasis is disrupted, which results in the production of the superoxide, hydrogen peroxide, enzymes like peroxidase, ascorbate peroxidase, & catalase,& non-enzymatic antioxidants like glutathione & ascorbic acid[19].
c) Heavy metals	Ni is a trace element necessary for the growth of plants, but too much of it prevents anthocyanins from accumulating, and trace metals restrict the production of anthocyanins by blocking the L-phenylalanine ammonia-lyase (PAL) activity.Up to 35% more oil content in Brassica juncea can be obtained by efficient metal production of Cr, Fe, Zn, and Mn.increased production of secondary metabolites like shikonin and are induced by Cu2+ and Cd2+, which also have an impact on digitalin synthesis. In Beta vulgaris, Cu2+ also promotes the synthesis of betalains. There are stimulatory effects of Co2+ and Cu2+ on secondary metabolite synthesis. While the concentrations of putriscine and spermidine in Helianthus annuus were lowered and those in beans and oats were enhanced by Cd2+ and Cu2+, the production of taxol by Taxus sp. was impacted by lanthanum.[20].
d) UV-B irradiation,heatand light intensity	Heat stress is known to increase the formation of stored ginsenosides but to decrease photosynthesis and biomass output. The generation of root secondary metabolites and leaf senescence in Panax quinquefolius was enhanced by heat stress. UV-B exposure increases the production of catharantine, vincristine, and vinblastine in Catharanthus roseus, which is used to treat leukaemia and lymphoma. In Populus xcanescense, however, changes occur to the transcript levels of genes involved to terpene biosynthesis. There has been evidence of a favourable relationship between light intensity and phenolic and flavanol levels. Shade-grown willows' leaves were found to have lower levels of phenolic glycosides & foliar tannin. A greater amount of anthocyanin accumulation was caused by modest amount of light (301 600 lx). Flavonoids in barley & polyamines in cucumber have been found to rise in response to UV-B light. UV-B[21].

e) Nutrient stress	Plant tissues have different phenolic levels depending on nutrient stress. Lignification and the buildup of phenylpropanoids are caused by deficiencies in phosphate and nitrogen. Under nutrient stress, quercetin-3-O-glucoside doubles and anthocyanidin levels in tomatoes increase threefold. Cautionary concentrations have been linked to reactions to several abiotic stressors, including as cold, drought, & salt stressors. Phenolic concentrations are also increased by deficiencies in potassium, sulphur, and magnesium. Tannic and flavonoid contents in Eugenia uniflora were both lowered by higher amounts of copper (Cu) and manganese (Mn)[22].
f) Climate change	Plants are slow to adjust to changing climate conditions and are quite sensitive to it. On the other hand, low levels of ozone exposure did not have influence on the amounts of resin acid and monoterpene., it did reveal enhanced conifer phenolic contents. Significant alterations in the chemical composition were seen in plants cultivated in elevated carbon dioxide (CO_2) environments. The drop in N concentration in grains, seeds, and vegetative plant parts, which in turn causes a decrease in protein levels, is a well-known example of the impacts of rising CO_2 levels. Research has indicated that leaves with higher CO_2 levels had more phenolics and condensed tannins. It was discovered that higher CO_2 in conifers affected the amounts of specific particular monoterpenes to decrease or rise while total phenolics increased.Under increased CO_2, monoterpene A-pinene levels climbed in coniferous breeds whereas B-pinene levels decreased.[23].

BIOTIC STRESS

When it comes to living organisms, plants have complex relationships with other organisms, such as microorganisms. These relationships can involve attracting pollinators or defending against insects and pathogens. In short, biotic effects on plants are all about how they interact with the living world around them[24-25].Features of plant physiology, including ontogeny and phenology are crucial in understanding the various cycles in plants. Phenology refers to the different cyclic activities that occur in plants, including ultradian, circadian, and infradian cycles. Ultradian cycles are defined as periods of activity that are longer than one hour but less than twenty-four hours, such as the expansion and contraction brought on by transpiration-induced variations in xylem pressure. Circadian functions, such as stomatal gas exchange, happen in a 24-hour cycle. Seasonal variations are part of the longer than daily recurrence time of infradian cycles. Conversely, ontogeny establishes the physiological variations that transpire during a live organism's existence[26]Plant development is characterised by discernible shifts in the concentrations of secondary metabolites, including hypericin, chlorogenic acid, and querceti . Hypericum origanifolium shows the highest levels of these compounds during the floral budding and full flowering stages. Similarly, H. brasiliense has the highest content of quercetin and rutin during the flowering stage, with a decrease in both compounds during fructification[27].Plant chemicals released by plants can also impact microbes, known as allelopathic chemicals[28].These substances, which include cyanogenic glycosides, flavonoids, alkaloids, terpenoids, and phenolics, are released into the environment by means of volatilization, leaching, decomposition of plant matter, and exudates from roots[29]. Allelochemicals can alter gene expression in nearby plants, interfere with signal transduction pathways, alter the composition of cell walls and membranes, affect seed germination, and raise the formation of reactive oxygen species.Allelochemicals have the advantage of aiding in plant adaptation by enhancing their capacity to withstand and withstand environmental stress[30].

GENETIC DIVERSITY

Genetic diversity plays a crucial part in identifying the chemotypes, or chemical profiles, of medicinal plants. This diversity can be seen across different levels: between different plant genera, within species of the same genus, and even within individual species through polymorphic variations. These variations can result in individual plants producing different dominant terpenes due to their unique genotypes.[31].A plant belonging to the Lamiaceae family called Thymus vulgaris is a prominent illustration of chemical diversity. This plant finds extensive application in both the food and cosmetics industries[32].Many medical conditions, including hair loss, oral plaque, dermatophyte infections, bronchitis, cough, inflammatory skin problems, and gastrointestinal discomfort, are reported to be alleviated by thyme. It contains anti-inflammatory, antifungal, and antibacterial properties. Depending on the predominant monoterpenoids present in its essential oils, thyme can have up to 13 distinct chemotypes and nine subspecies[33]. Analyzing the genetic diversity among plant varieties is important for pinpointing the ones that have desirable traits for agricultural purposes. This data is valuable for initiatives aimed at enhancing crop quality and productivity[34].

ADULTERANTS

"Many times, impurities can be found in medicinal plant material in the form of adulterants.Adulterants are compounds with biological activity or unidentified chemicals that are purposefully introduced to medicinal plant substances in order to increase the potency of the plant-based remedy. This is an unlawful and dishonest conduct[35]. There is an increased danger of contamination when raw or semi-processed conventional drugs in many poor nations are sold in muthi stores and open public markets without labelling or packaging[36].It's crucial to adhere to quality control procedures like GMP for herbal remedies and GACP for medicinal plants in order to prevent contamination[37-38]

ADVERSE CONSEQUENCES

An adverse reaction is when your body has a negative response to a medication or other substance that is not intentional, occurring at typical human doses for treatment or diagnosis of an illness, or for altering bodily functions[39].Plant-based health goods and medicinal plants are viewed as pure and natural by locals and customers of health stores that sell herbal remedies. They consider these goods to be risk-free, safe, and without any negative side effects.[40-41].Plants have developed chemical defenses to help them survive. These defenses are natural compounds found in plants that are used to protect against threats from other plants and animals by deterring, stunning, poisoning, or killing them. It is important to remember that plant extracts may not always be safe for humans to use[42]. Particularly concerning are the nitrophenanthrene carboxylic acid compounds called aristolochic acids, which occur naturally in plants of species like Aristolochia & Asarum in the family Aristolochiaceae that have the capacity to induce mutagenesis and cancer[43].

VARIABILITY Of CHEMICAL COMPOUND CONCENTRATION

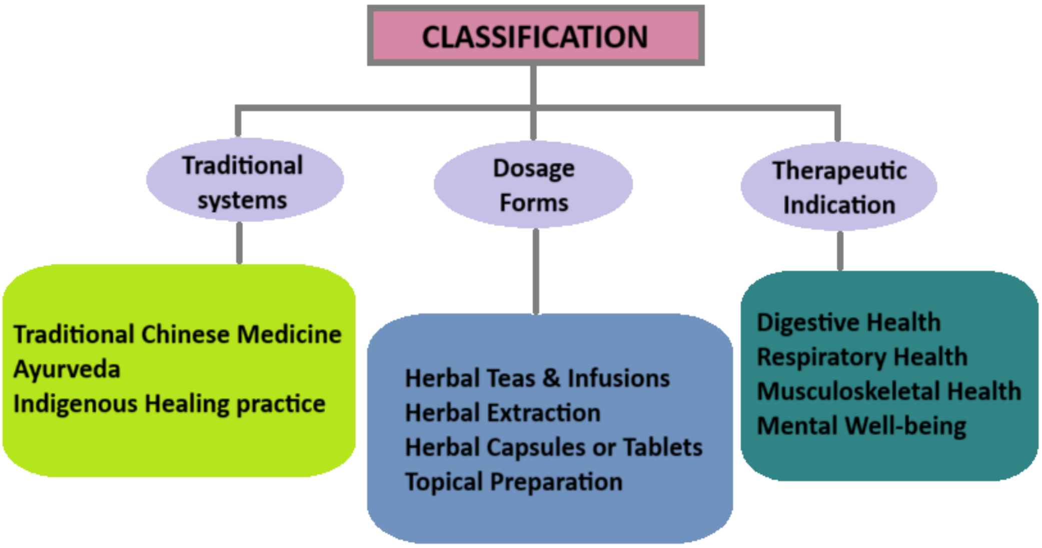
The fluctuation of the chemical compound content in the medicinal plant material has not received enough attention.Dosage application and chemical component concentrations in plant material are related. There is a chance that any chemical could be poisonous.A medicine can be distinguished from a poison based on the dosage used[44]. Taking excessive amounts of medicine, whether it is plant-based or Western, is best avoided.[45]. However, the intended outcome might not be achieved by underdosing. Drug/herbal medication interactions, the patient's condition, age, and weight, should all be considered when traditional health practitioners prescribe traditional medicines[46]. Prescription dosages and the usage of complementary therapies are frequently not standardised or subject to regulations. Thus, there is always a chance of poor administration[47].

Table 2: classification of the main impurities and leftovers in herbal remedies [48]

General Classification	Group	Subgroup	Specific examples	Possible sources	Stage of production at which detection occurred
Chemical Contaminants	Hazardous & toxic materials	Toxic metals and non-metals	Lead, mercury, chromium (arsenic, nitrite)	Polluted soil and water, during cultivation/ growth, manufacturing process	1 - 4
		POPs	Dioxin, chlordane, DDT, dieldrin,	contaminated water, soil, and air during	1 - 4

		Radionuclide Biological toxins	endrin,heptachlor, mirex Cs-134, Cs-137 Mycotoxins Bacterial, Endotoxins	cultivation and growth Air,soil,and water during cultivating or growing Post-harvest handling, transportation, and storage Post-harvest handling, transportation, and storage	1 - 4 2 - 4 1 - 4
Biological Contaminants	Microorganis-ms Animals	Bacteria Fungi Parasites Insects Others	Staphylococcus, Pseudomonas aeruginosa,Salmonella species, Shigella species, Escherichia coli Yeast, moulds Protozoa - amoebae, Helminths - nematode Cockroach and its Parts Mouse excreta, earthworms, acarus	Soil, processing after harvest, transportation, and storage Post-harvest handling, transportation, and storage Excreta, soil, organic cultivation, and manufacturing methods Post-harvest handling, transportation, and storage Post-harvest handling, transportation, and storage	1 - 4 1 - 4 1,3,4 1,2,4 1,2,4
Solvents	 Pesticides	Organic Solvents Insecticides Herbicides	Acetone, methanol, ethanol, butanol Carbamate, chlorinated hydrocarbons, organophosphorus 2,4-D, 2,4,5-T	Soil and water, during cultivation/growth, manufacturing process air, soil, and water; during cultivation and growth; and during the post-harvest processing air, soil, and water; during cultivation and growth; and during the post-harvest processing	1 - 4 1 - 4 1 - 4
Agrochemical Residues	 Fumigants Disease control Agents	Fungicides Chemical agents Antiviral agents	Dithiocarbamate Ethylene oxide, phosphine, sulphur dioxide Thiamethoxam	air, soil, and water; during cultivation and growth; and during the post-harvest processing Post-harvest processing During cultivation	1 - 4 2 - 4 1 - 4
Residual solvents	_ _	Organic Solvents	Acetone, methanol, ethanol, butanol	Manufacturing process	3,4

PRODUCT CLASSIFICATION FOR HERBAL MEDICATIONS



QUALITY CONTROL FOR HERBAL MEDICATION ITEMS

Herbal product creation, production, and distribution are all subject to systematic supervision and control measures known as quality control, which are designed to ensure a constant level of product quality[49]. Any industry or organisation must have quality control procedures since they are crucial to ensuring that goods and services fulfil the required standards and requirements[50,51].Organisations can increase productivity and produce more with less resources by optimising operations, removing bottlenecks, and correcting inefficiencies[52].

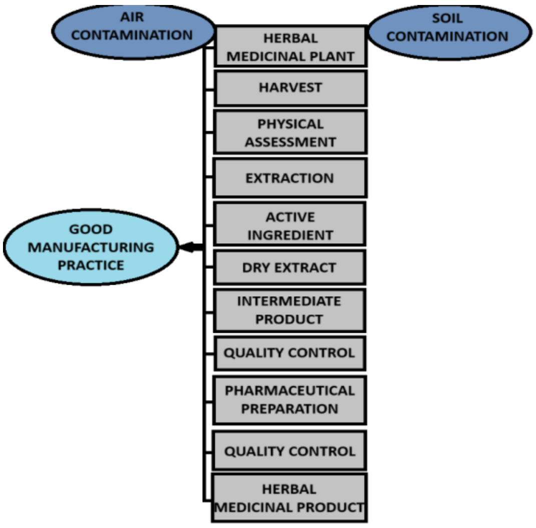


FIGURE 1:- The progression of herbal remedies to their products and potential sources of contamination

Herbal identity and standardisation

Establishing identification and standardisation of herbs is the first step towards implementing efficient quality control procedures. Establishing reliable as well as consistent methods is necessary for the standardisation and recognition of herbs. concentrations of markers potentially active ingredients in goods made with herbs[53].

discover the herb's main active ingredients and/or indicators that are standardised and contribute to its medicinal qualities. They can be accomplished by scientific study, conventional wisdom, or already published material. Some important components of them are active compound verification, qualitative evaluation, and guidelines for reference[54].

Develop quantitative methods for measuring the concentrations of markers or active substances [55]. Chromatography (HPLC, GC), spectroscopy, and other approaches may be used for this. according to[56], or certain chemical tests (UV-Vis, IR). A reference material or standard that represents the appropriate concentrations of active chemicals or indicators should be established [57]. According to [58] these standards provide consistency between batches by providing standards of reference for assessment in quality control tests. Healthcare practitioners may safely administer treatments when a framework for standardising the monitoring and control of the effectiveness and quality of herbal medicinal products is in place.

Authenticity testing techniques are essential to control of quality for herbal medicinal items since different plant species or sections may have distinct therapeutic advantages as well as safety profiles. They ensure that the correct herb is being utilised by providing precise verification and recognition of the herbs used[59]. Identifying botanical varieties or plant parts utilised in herbal medical products with accuracy is the technique of herb identification [60]. A few often used techniques for authenticity testing are chemical profiling, thin-layer chromatography(TLC), high-performance liquid chromatography(HPLC), microscopic inspection, and DNA barcoding.

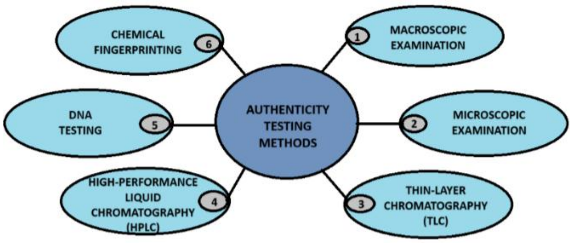


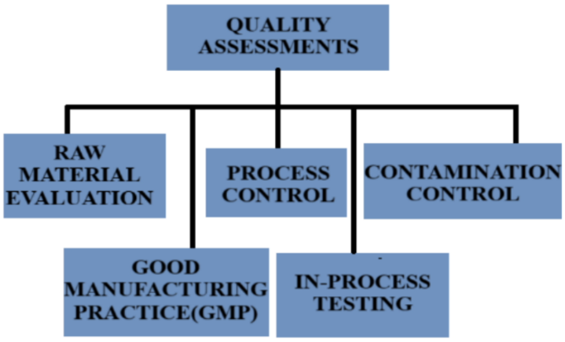
FIGURE 2:-Methods used for quality control that provide precise identification and validation of the herbs.

MANUFACTURING AND PROCESSING CONTROLS

One of the most important steps in creating herbal medication products is using effective extraction methods to obtain the necessary active ingredients found in herbs [61,62].Regarding the extraction and optimisation processes for herbs, there are a number of critical aspects to take into account. These comprise selecting the appropriate solvent, appropriately preparing the herbal material, figuring out the appropriate ratio of solvent to materials, managing temperature & extraction durations, applying different extraction methods, carrying out several extractions, modifying pH levels, adding co-solvents or boosts, guaranteeing control over quality, giving priority to safety precautions, aiming for long-term viability and confirming validation and reproducibility[63,64]To ensure that the outcomes are reliable and consistent, validation of the extraction procedure is crucial after it has been established.This validation comprises making sure that certain quality requirements, such extraction yield, efficiency, and the presence of required bioactive chemicals, are constantly met by the extraction process.[65,66]. "Validation parameters can consist of conducting analytical tests, comparing against reference samples, and performing statistical analysis"[67,68].

EVALUATION OF QUALITY IN THE PROCESSING PHASE

Evaluating the quality of herbal medicine goods is essential for ensuring their safety, effectiveness, and consistency during processing[69]. It is essential to monitor and assess several characteristics and aspects during the production process.[70]. Here, A few assessments of quality were compiled while processing.



CONCLUSION

In many developing countries, traditional medicines are the primary choice for healthcare. But plant-based health products are becoming more and more popular, especially in industrialised nations. There is a lack of consistency in the plant material accessible in the market due to a variety of biotic and abiotic variables that affect plants' ability to produce secondary metabolites. Despite having labels, over-the-counter health items sometimes don't include important details regarding their bioactive ingredients, concentrations, and recommended or contraindicated uses.This may lead to erratic dosage and perhaps harmful consequences.Many traditional stores and open-air marketplaces sell a wide variety of medications without labelling or packaging.This leaves them open to biological and chemical pollutants that may compromise the efficacy of herbal and plant-based therapies.A couple of these toxins can be extremely harmful, originating from either natural sources or human activities. There have been instances of iatrogenic side effects from using conventional medications.It is important to follow guidelines for collecting and handling plants after they have been harvested in order to avoid contamination of plant products that are used for medicine or food. Regulatory agencies should prioritize activities such as screening, standardizing, packaging, labeling (including providing warnings when needed), and registering and licensing plant-based medicines.These steps are required to guarantee that customers may obtain health goods which are effective as well as secure.

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