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TOXICITY OF SOME HERBAL MEDICINE: NEED OF TOXICITY TESTING AND SEAFTY OF HERBAL MEDICINE.

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Abstract **-** In every country traditional medicine find foundation in magical or religious belief and considered as safe and free from undesirable side effect. Herbal products are not evaluated for purity and consistency of active constituent they also contain some contaminant. With the increased use of herbal products, the safety and efficacy of herbal medicine are being questioned. Recently some herbs show toxicity such as Glycyrrhizin glabra Linn, Ginkgo biloba, Panax ginseng, Allium sativum, and more herb. Adverse health effects linked to herbal products could be related to both the inevitable harmful effects of medicinal herbs and toxicities caused by adulterants/contaminants. The lot of evidence regarding the side effects of herbal medicine has emphasized the requirement for and importance of toxicity studies for herbal products. Toxicology plays a major role in the development of herbal medicines. Thus the safety criteria are important in development of herbal medicine for saving life of human. The present review focused on need of toxicological study and safety of herbal drug prior to used. The toxicity studies need to be done even plant have long history of drug usage or do not have any documented toxicity so they can lead some unrelated toxicity especially during long term treatment for chronic condition or when used as food supplement.

Key word **-** Allium sativium, Glycyrrhiza glabra, herbal drug, herbal toxicity

INTRODUCTION

Herbal drug

Herbal medicine is the therapeutic use of plants, plant parts, water or solvent extracts, essential oils, gums, resins, exudates, or other advanced products made from plant parts to provide proactive support of various physiological systems; or, in a more traditional medical sense, to treat, cure, or prevent disease in animals or humans [1]. There has been a recent shift in the global trend away from synthetic medicine and toward herbal therapy, which we might call a "Return to Nature." Medicinal plants have been valued for millennia as a rich source of therapeutic compounds for the prevention of diseases and ailments all over the world. The assumption that all natural goods are safe is one reason for their appeal and acceptance. Plant-based medicines, health products, pharmaceuticals, food supplements, cosmetics, and other natural products are in high demand in both developing and developed countries, thanks to a growing awareness that natural products are non-toxic, have fewer side effects, and are readily available at low prices. Since the dawn of time, people have been searching for natural treatments for ailments. [2] In recent years, herbal remedies have gained appeal in dietary supplements, energy drinks, multivitamins, massage, and weight loss treatments. [3].

NEED OF TOXICITY TESTING OF HERBAL MEDIINE

Natural therapies are now the basis for pharmaceutical pharmaceuticals. Traditional herbal remedies are naturally occurring plant-derived substances that are still utilised to treat and cure a variety of diseases, disorders, acute and chronic health problems, and as nutritional supplements in the twenty-first century. Herbal medications are widely accessible on the market around the world and come in a number of forms. [3a] As the usage of herbal medicinal items expands around the world and more innovative goods enter the market, public health problems emerge. Interest in drugs generated from higher plants, particularly phytotherapeutics, has grown dramatically during the last decade. Higher plants are thought to be the source of around 25% of all contemporary medications, either directly or indirectly. [4] According to the World Health Organization,

about 70-80 percent of the world's population, primarily in developing nations, uses non-conventional medicine produced from plant material in their primary healthcare (WHO). [5] Synthetic drug-related adverse or side effects account for about 8% of hospital admissions in the United States. [6] As individuals in the western world become more aware of the potency and side effects of synthetic drugs, interest in natural therapies with a more basic approach to nature is growing, resulting in a surge in herbal medication manufacturing. [7] Drug toxicity testing is a source of concern for the sake of safety. There must be no toxicity in any of the medications used in the research. [7a] Herbs are not subject to the same pre-market testing as pharmaceuticals and food additives because they are designated as dietary supplements rather than foods or drugs. Toxicology testing is carried out to obtain information about the drug's safety as well as to assess its biological activity and mechanism of action. The test's results are used to identify potential medication hazards and control risk. [7b]

AN APPROACH TOWARDS HERBAL DRUG'S TOXICOLOGICAL STUDY

Natural medicines have clearly risen in popularity and acceptance in both developing and developed countries over the last decade, with herbal medications now available not only in drug stores but also in grocery stores and supermarkets. Many problems in primary care are caused by a lack of understanding and sensitivity to local health behaviours, as well as the economic and cultural variables that influence these practises. However, there is no clear statement of substance or medically relevant information on the package labels of available herbal products, and they have not been validated or certified by any recognised agency. This is concerning for both consumers and medical professionals who may unintentionally prescribe these natural products. Not all plants that are said to be beneficial are safe. [8] Complementary and alternative therapies have become increasingly popular in recent years. [9] For preventive or palliative treatment, an increasing number of patients are turning to herbal medicines; on the other hand, herbal medical products are becoming increasingly popular around the world. Herbal medicine is still poorly understood by the general public, medical practitioners, the scientific community, and the media all around the world. In most cases, lack of experience, education, and other conventional health care practitioners are suspicious and uncomfortable, especially when their patients are taking exaggerated claims of miracle cures and unproven medicines [10]. Herbal remedies are made up of parts of plants or unpurified plant extracts that contain several constituents that are often thought to work together. The presence of mixtures of biologically active plant constituents or phytochemicals (secondary metabolites) such as alkaloids, glycosides, terpenoids, and others that may act individually, additively, or synergistically to demonstrate efficacy is the basis for the medicinal use of plants. Some of these plants have been classified as poisonous plants due to their effects on biological activities in other creatures, which can be dangerous when used in excessive doses or on a regular basis. [11] As the global use of herbal medicinal goods grows and more novel items enter the market, public health issues and concerns about their safety are becoming more widely recognised. Although some herbal medications have a lot of promise and are extensively used, many of them haven't been evaluated and their use hasn't been supervised. This limits our understanding of their possible side effects and makes identifying the safest and most effective therapies, as well as encouraging their reasonable use, more challenging. [12] We lose sight of reality when we think of herbal medicine as either a panacea or a poison. Although just a few of the herbs listed below have a long history of medical usage, they have been shown to be poisonous.

TOXICITY OF SOME HERBAL PLANT

1.Glycyrrhiza glabra (licorice)

Glycyrrhiza glabra is one of the most well-known medicinal plants in the Fabaceae (formerly known as Leguminosae) family, and its relatives are now widely utilised as feed and food. This species is endemic to the Mediterranean region, although it has recently spread to India, Russia, and China. Currently, the extracts are employed in the pharmaceutical and food industries, as well as in the production of functional foods and food supplements. [13] Glycyrrhiza glabra roots contain several active compounds flavonoids, such as liquirtin, rhamnoliquirilin, liquiritigenin, prenyllicoflavone-A, glucoliquiritin apioside, 1-metho-xyphaseolin,
shinpterocarpin,shinflavanone,licopyranocoumarin,

glisoflavone, licoarylcoumarin, coumarin-GU-12 and saponins namely glycyrrhizin (60 times more sugary than sugarcane).In addition, four isoprenoid-substituted phenolic constituents (isoangustone-A, semilicoisoflavone-B, licoriphenone, and 1-methoxyficifolinol), kanzonol R (prenylated isoflavan derivative) and several volatile components (pentanol, tetramethyl pyrazine, hexanol, terpinen-4-ol, linalool oxide A and B, geraniol, and α-terpineol) have also been reported. Whereas propionic acid, 1-methyl-2-formylpyrrole, 2,3-butanediol, benzoic acid, ethyl linoleate, furfuryl formate, trimethylpyrazie, furfuraldehyde, methyl ethyl ketone, and maltol were isolated from the essential oil. Glycyrrhizin a saponin compound as well as its aglycone glycyrrhetinic acid, are the potent components in Glycyrrhiza glabra. Glycyrrhizin is made up of glycyrrhetic acid, triterpenoid aglycone, and glucuronic acid disaccharide, and it's present in licorice root as calcium and potassium salts. [14,15,16] Licorice is one of the world's oldest and most widely used natural medicines. Many of the historical uses of liquorice are still used today. It's used to treat a variety of medical conditions, including asthma and other lung disorders. It also acts as an antitussive. [17] Glycyrrhiza glabra has antifungal properties. As a result, licorice extract has a lot of potential in cosmetics with antibacterial properties. [18] It's also used to treat the cancer of various kinds. The anticarcinogenic and antimutagenic action of G. glabra against the human cervix and uterus tumour cell line SiHa cells was demonstrated due to its 18glycyrrhetinic and glycyrrhizic acids that promote mitochondrial permeability transition, leading to tumour cell demise. [19] Glycyrrhizin and glycyrrhezinic acids are beneficial in the treatment of gastric cancer, while glycyrrhizin reduces thromboxane A2 in lung cancer cells with little side effects. [20] Liquorice promotes hair development and can be used safely in herbal formulations to treat alopecia. [21] Glycyrrhizin has a low oral bioavailability and is only found at very low concentrations after a single oral intake. Glycyrrhizin can be converted to glycyrrhetinic acid in humans. Glycyrrhizin shares many of the same pharmacological properties as glycyrrhetinic acid. [22] Glycyrrhizic acid and glycyrrihetic acid, among other metabolites, are responsible for licorice's pharmacological actions (glycyrrhetinic acid). [23] Glycyrrhetic acid is a triterpenoid aglycone conjugated to glucuronide and sulphate that is 200–1000 times more effective than glycyrrhizic acid as an inhibitor of 11b-hydroxysteroid dehydrogenase (11b-HSD) and has a spectrum of corticosteroid-like actions. [24] Several clinical investigations have highlighted scientific evidence connected to licorice's pharmacological qualities, such as hepatoprotective, [25,26] anti-inflammatory, [26-28] antiviral, [26] anti-ulcer, [29] and immunoregulatory activities. [28] However, the general consensus is that licorice is a safe, natural herb with no major side effects. This notion could lead to excessive use or misuse of glycyrrhizin, both of which could be dangerous. Apart from glucocorticoid-like activity, liquorice can cause mineralocorticoid-like over activity through inhibiting 11b-HSD as well as binding directly to mineralocorticoid receptors (MRs). [30] As a result, long-term high-dose glycyrrhizin exposure may cause mineralocorticoid excess and subsequent inhibition of the renin–angiotensin–aldosterone pathway. [31] Hypokalaemia, metabolic alkalosis, cardiac arrhythmia, oedema, hypertension, and other undesirable consequences linked to its mineralocorticoid-like activities could result from this exposure. [32] Physiologically, the 11b-HSD2 enzyme converts cortisol to inactive cortisone, preventing it from binding to the MR. [33] By blocking the 11b HSD2 enzyme, glycyrrhizic acid raises cortisol levels. Hypokalaemia, metabolic alkalosis, cardiac arrhythmia, oedema, and hypertension are all symptoms of licorice-induced pseudoaldosteronism. Individuals using high dosages of glycyrrhizin-based medications or consuming substantial amounts of licorice-containing health items over a lengthy period of time had low plasma renin activity and aldosterone.

Toxicity

Leskinen et al. [34] found that eating licorice for two weeks increased extracellular volume and raised systolic and diastolic blood pressure (DBP). [34] Licorice consumption raises blood pressure through increasing extracellular fluid volume and major artery stiffness, according to Hautaniemi et al. [35]. [35] Chronic licorice consumption raises blood pressure (5.45 mmHg for SBP and 3.19 mmHg for DBP) and lowers serum potassium levels, according to a meta-analysis of 18 trials (n=337). [36] Glycyrrhetinic acid, the active component of glycyrrhizin, has a mineralocorticoid-like activity that can directly affect the kidney or indirectly boost the effect of aldosterone. [36] As a result of increased Na+ resorption in the distal tubules, K+ excretion is increased, resulting in hypokalaemia and water retention.

Because of the danger of cardiac arrhythmias and prolonged QT intervals associated with severe hypokalaemia in the high-risk category, close monitoring of blood potassium levels and electrocardiography is essential. Rhabdomyolysis, acute tubular necrosis, asthenia, and muscular cramping are all rare but possible side effects of licorice. [24]

2. Ginkgo biloba

The Ginkgo biloba tree (ginkgo, family: ginkgoaceae) is thought to be one of the world's oldest living species of tree. This tree is native to China and has been cultivated as an ornamental tree all over the world. Ginkgo leaf extracts are commonly found in herbal medications, food and dietary supplements, as well as botanical and complementary therapies. A variety of bioactive compounds such as terpenoids (e.g., ginkgolides, bilobalide), flavonoids (e.g., kaempferol, quercetin, isorhamnetin), biflavonoids (e.g., sciadopitysin, ginkgetin, isoginkgetin), and organic acids (e.g., ginkgolic acid), among others, broaden its use in different biological system [37] Ginkgolide A, Ginkgolide B, Ginkgolide C, Bilobalide, Ginkgotoxin, ginkgolides and are the major constituents. Ginkgolides can be classified in five forms (A, B, C, J, and M) Ginkgolides A, B, and C, and bilobalide have been shown to increase circulatory perfusion, antagonize platelet activating factor (PAF), have neuroprotective effects, and serve as cognitive activators. The flavone glycosides possess antioxidant and mild platelet aggregation inhibiting activities [38-39] Ginkgo trees are currently widely grown throughout Asia, Europe, North America, New Zealand, and Argentina. [40] Ginkgo biloba is used to treat a variety of ailments. A number of scientific research on the pharmacological properties of Ginkgo biloba have revealed a variety of pharmacological activities, including. Hepatoprotective [41] The ginkgo tree is a deciduous tree with green leaves that become golden in the autumn, and ginkgo seeds are found in ginkgo fruits produced by female trees. Cough, asthma, enuresis, pyogenic skin diseases, and intestinal tract worm infections have all been treated with the nut-like gametophytes found inside the seeds in traditional Chinese medicine. [42] Memory loss and cognitive impairments, arrhythmias and ischemic heart disease, cancer, diabetes, and thromboses have all been treated with ginkgo leaves. [43]

Toxicity

Spontaneous bleeding has been linked to the usage of Ginkgo biloba leaf extract, albeit there are conflicting research findings. A routine postoperative ultrasound detected a likely sub capsular hematoma around the dome of the liver, as well as a vitreous haemorrhage in his right eye, in a 59-year-old Korean man who had a liver transplant. [44] The activation of CYP enzymes in humans by Ginkgo biloba leaf extracts has been described in several studies, shedding light on potential interactions between ginkgo and conventional medicines. A 55-year-old male patient died in the United Kingdom after suffering a breakth The anticonvulsants, valproate, and phenytoin serum levels were found to be below therapeutic levels in the postmortem report. Because both anticonvulsants are metabolised by cytochrome P-450 2C9 (CYP2C9) and 2C19 (CYP2C19), and because ginkgo can increase CYP2C19 activity, extensive anticonvulsant metabolism due to CYP2C19 induction and the effect of the potent neurotoxin MPN on the seizure could be a plausible explanation. [45] In a review of case reports of herb-induced seizures, Samuels and colleagues postulated three pathways for ginkgo-induced seizures: participation of MPN, inhibition of platelet activating factor, and activation of CYP2C19. [46] rough seizure with no evidence of noncompliance with his anticonvulsant meds. His physician revealed that a year before his death, he had begun using herbal supplements (Ginkgo biloba, ginseng, and saw palmetto extracts) and non-prescription vitamins.

3 Allium sativium

Garlic (Allium sativum L.; Amaryllidaceae) is an aromatic herbaceous annual spice and one of the oldest authenticated and most important herbs used in traditional medicine from ancient times. [47,48] Garlic has long been used in cooking as a spice to flavour items while they are being prepared. Garlic can be found growing wild in Central Asia, Southern Europe, and the United States. In India, it is widely grown. [49] Hundreds of phytochemicals, including sulfur-containing compounds, have been found in Allium.sativum bulbs such as as Alliin, ajoenes (*E*-ajoene, *Z*-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H) -1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS)) and others that accounted 82% of the overall garlic sulfur content.[50]

Allicin [S-(2-propenyl)-2-propene-1-sulfinothioate], the most biologically active sulfur-containing compound of garlic, is responsible for its smell and taste. [51,52] Alliin (S-Allyl-L-cysteine sulfoxide) is the most important precursor to allicin, accounting for over 70% of total thiosulfinates in crushed cloves. [53] Garlic has been used as a medicine to treat a variety of ailments and conditions due to the presence of its biological active component allicin and its derivatives. Garlic and its associated components have traditionally been thought to have anticarcinogenic, antioxidant [54], antidiabetic, renoprotective, and anti-atherosclerotic properties. antibacterial and antifungal properties [55] Garlic has also been used in traditional medicine to treat indigestion, respiratory and urinary tract infections, and cardiac diseases, and it has been shown to have carminative, antipyretic, sedative, aphrodisiac, and diuretic properties. [56] Garlic has been shown to have impacts on hyperlipidaemia, hypertension, and platelet aggregation, all of which are CVD risk factors. [57] Allicin, which is formed when the garlic clove is crushed, is primarily responsible for its anti-atherosclerotic abilities. were able to demonstrate that allicin can influence atherosclerosis through a variety of mechanisms, including lipoprotein alteration and suppression of LDL uptake and breakdown by macrophages [58]. By inhibiting 3hydroxy-3-methylglutaryl (HMG)-CoA reductase and 14--demethylase, allicin and ajoene were reported to drastically limit cholesterol production [59].

Toxicity

Long-term feeding of high quantities of raw garlic to rats resulted in anaemia, weight loss, and failure to grow due to red blood cell lysis, according to animal research. [60] A dose of 5 ml/kg of raw garlic juice resulted in mortality owing to stomach damage. [61] In rats, chronic treatment of garlic powder (50 mg/day) inhibited spermatogenesis. Garlic's anti-androgenic actions are reflected in lower levels of sialic acid in the testes, epididymis, and seminal vesicles, as well as decreased lending cell function. [62] There have been reports of allergic contact dermatitis caused by topical or oral therapy with garlic. A 78-year-old Major appeared with widespread eczema and a history of volar hand eczema. The patient had been scratching the uncomfortable dry skin of his lower legs four months' prior, resulting in excoriations and tiny erosions, particularly on his left leg. His wife used hydrocortisone cream and emollients on his legs, but she also used crushed garlic cloves diluted in water as a wet dressing on occasion. The dermatitis worsened over time, spreading over his trunk and arms. When testing with no irritating quantities of garlic powder and diallyl disulphide, allergic contact dermatitis was established. [63] German and colleagues described the case of a 72-year-old man who was catheterized after being admitted with acute urine retention. He wasn't taking any medications other than garlic tablets, which he'd been taking for years for medical reasons. He had transurethral excision for prostatic benign hyperplasia four days later. The resection was "bloody," with only modest haemostasis. He had a second cystoscopy 4 hours later due to the continued haemorrhage. There were no specific bleeding spots discovered during the procedure, but there was a general oozing from the entire prostatic cavity. He received four units of blood and recovered well. Platelet function tests were done three months after he resumed his regular dose of garlic tablets. Platelet aggregation failed in the presence of collagen in these tests, indicating a platelet coagulation deficiency. [64]

Reported adverse effect (toxicity) of some herbal medicine listed below

Sr.no	Herbal medicine	Uses	Side effect
1.	*Cats claw (Uncared tomentosa or U. guianensis) CKLS (colon, kidneys, liver, spleen)*	Anti-inflammatory agent, systemic lupus erythematosis.	Acute allergic interstitial, nephritis, unilateral acute tubulo interstitial nephritis, diarrhoea, abdominal pain, haematuria.
2.	*Lei Gong Teng (Tripterygium wilfordii)*	Anti-inflammatory and rheumatoid arthritis	Profuse vomiting, diarrhoea, hypovolemia, ARF, shock, death[65]

3.	*Oduvan (Cleistanthus collinus*	Abortifacient and is known to be toxic, not medicinal.	Hypokalaemia, hypotension, arrhythmias, ARF and death[66]
4.	Ting Kung Teng (Erycibe henryi)	Purgative, low-dose exert cholinergic and sedative actions.	Severe hypotension, increased BUN, creatinine and metabolic acidosis. heart toxicities included hypertension, hypotension, hypokalaemia, bradycardia, tachycardia, arrhythmia, ventricular fibrillation, heart attack, cardiac arrest, heart failure, and death[67]

Reported adverse effect (toxicity) of some herbal medicine listed below [68]

Sr. no	**Scientific names Species names** Family	**Used part**	**Medicinal uses**	**Toxics compounds**	**Toxicities**
1	*Aconitum vulparia Renonculacae*	Root	Analgesic; Antirheumatic; Anticongestif; Against sciatic and teeth pain	Aconitine	Vertigo; Diarrhoea; Hypertension; Shivering Tachycardia; Respiratory paralysis
2	*Aristolochia longa Aristolochiacoe*	Roots	Against intestinal pain; Diuretic; Cutaneous diseases; Cataplasm against snake	Aristolochic acid	Nephrotoxicity; Carcinogenic effects; Alteration of liver and kidney enzymes; Damage liver and kidney
3	*Anagyris foetida Legumineusea*	Seeds	Against eczema; Purgative; Against renal disease; Emetic	Anagyrine (alkaloid)	Tachycardia; Hypertension; Vomiting; Diarrhoea
4	*Atropa belladona Solanaceae*	Roots Leave	Narcotic; Diuretic; Antispasmodic; Treatment of eye diseases; Antidote of opium; As lotion; Rheumatism and sciatic; Giving in collapse of	Troponic acid, EsterTropanol ,(scopariol) Atropine Hyoscia-mine(alkaloid), Scaplomine, Starch Belladonine (apoatropine)	Nervous system intoxication.

			pneumonia; Typhoid fever		
5	*Bryonia dioica Cucurbitacae*	Roots Fruits	Against dysentery; Purgative; Against ulcer	Cucurbitacin (tetracyclic diterpen) Brydiofin	Titanic convulsion; Hypothermia; Cramp; Coma.
6	*Citrulus colocynthis Cucurbutacae*	Fruits Seeds	Antidiabetic; Against blenorrhagia	Elatermidine, Glycosides, Resin, Dihydric alcohol, Heltiacontane, Citrullin, Citrullinic acid	Gastrointestinal pain; Diarrhoea; Vomiting; Hypothermia; Cardiac disorder; Cerebral congestion; Necrosis of liver and renal cells.
7	*Colchicum autumnal Liliaceae*	Seeds Capsule	For rheumatism; Arthritis; Sedative; Act upon all secreting organs particularly the bowels and kidneys	Colchicine (alcaline substances)	Vomiting; Diarrhoea; Antimitotic; General paralysis; Respiratory paralysis.
6	*Datura stramnium Solanaceae*	leaves	Antispasmodic; Emollient; Narcotic; Against asthma; Palliate the pain; Muscle rheumatism; Neuralgia; Hemorrhoid; Fistula; Abscesses; Inflammation	Hyosciamine (alkaloid), Atropine, Hyoscine, Malic acid, Daturin (mixture of hyosciamine and atropine)	Serious neuralgic; Hallucination
7	*Digitalis purpura*	Leaves	Diuretic; Cardiotonic; For cardiac arrhythmias oedema; Oliguria	Digitalis, Glycosides, Digitoxin, Digitalin , Digitalein ,Digitonin	Cardiovascular, neurological and digestive troubles; Hallucination; Photophobia; Exophthalmia
8	*Iris pseudoacorus Iridacae*	Rhizome	Emetic; Purgative; Rubefacient Against sneezing.	Irisin ,Iridin	Abdominal pain; Nausea, Vomiting; Diarrhoea; Spasm; Staggering; Paralysis

9	*Mandragora automnalis Solanacea*	Leaves	Against asthma and cold; Narcotic; Anaesthetics; Appetizing	Atropine Hyosciamine Scopolamine	Death
10	*Withania somnifera Solanacea*	Seeds Roots	Narcotic; Sedative; Antiepileptic; Diuretic; Light laxative; Abortive	Alkaloids	Vomiting; Tetanic convulsion; Mydriasis
11	*Taxus baccata Taxaceae*	Leaves	Treatment of rheumatism	Cyclitols; Fatty acid; Stérols, bisflavonoids, ProanthoCyanidols, Lignanes ,Cyanogenetic Heterosides;Terpens	Paralysis of cardiac and pulmonary functions; Hypotension; Respiration depression; Vomiting; Nausea; Diarrhoea; Abdominal pain; Convulsion; Coma
12	*Thapsia garganica Compositae*	root	Against rheumatism; Bronchitis; Feminine sterility	Resin	Vomiting; Violent diarrhoea; Digestive mucous inflammation; Salivary secretion; Nervous disorder; Violent colic; Gastroenteritis; Death

SEAFTY OF HERBAL MEDICINE

Despite the numerous benefits linked with folkloric medicines, the major concern is their safety for public health. Traditional healers' archaic practices are neither modern nor scientific, thus there is a considerable risk of germs and heavy metals contamination in herbal products, which could harm people's health. [69] Despite the numerous benefits linked with folkloric medicines, the major concern is their safety for public health. Traditional healers' archaic practices are neither modern nor scientific, thus there is a considerable risk of germs an as a result, the appropriate government must issue a directive on how to safeguard the public from the harmful consequences (including death) of using or abusing herbal products. Microbial contamination of herbal medications is frequent, and traditional healers find it difficult to avoid or manage this contamination. As a result, some quality control measures should be recommended in their practices, as well as possibly raising awareness about the potential health concerns linked with the use or abuse of herbal combinations. [70-72] In the formal herbal sector, toxicity issues with medicinal plants may be due to a lack of quality assurance and non-compliance with good manufacturing practice requirements. [[73] In addition, there is a lack of access to the information needed for efficient herbal medicine use, as well as incorrect methods to their use. Adulteration of herbal treatments with synthetic medications and other potentially harmful chemicals such

as other botanicals, pathogenic microbes, poisons, pesticides and fumigants, agrochemical residues, or heavy metals could exacerbate the problem. [73] The bulk of adverse occurrences associated with the use of herbal products are caused by inadequate quality control methods, which result in either poor product quality or a lack of product safety. [73] Poor regulatory mechanisms and mainly uncontrolled distribution routes, according to WHO, could contribute to such catastrophes. Adulteration of herbal products with other undeclared drugs and strong pharmaceutical chemicals like corticosteroids and non-steroidal anti-inflammatory agents, for example, results in low quality products. [73] Identifying actual adverse reactions to herbal medicines and herbal items is typically difficult until the reason of such events is determined. Herbal medicines are typically safe when used correctly. Their safety and efficacy have been established over time, with experience passed down from generation to generation.

CONCLUSION

Medicinal plants and herbal medicines are becoming increasingly popular, and they play an important role in human health around the world, particularly in underdeveloped nations. Since of the general public's lack of scientific education, many people believe that herbal treatments are safe because they are natural. Toxicological studies, on the other hand, have shown that plant products are potentially hazardous, posing a risk to their use. A number of variables could be to blame for the possibility for toxicity: a variety of ingredients, some of which may be innately harmful, such as tropane alkaloids and cardiac glycosides, notwithstanding their usage in traditional medicine. Also, it is noted that the route of administration and dose, of any chemical, are important regarding safety due to chemical or pharmacological interactions; this is undergirded by the need for a regulatory regime for quality. Serious adverse effects of therapies involving aqueous traditional medicines are rare. However, efforts to investigate toxicity, organ toxicity and cytotoxicity, have involved the use of organic solvent plant extracts and routes of administration which constitute a drawback to the conclusions drawn from such studies. Information on the traditional formulation and use of the herbal medicines should be satisfactory to avoid possible toxicity from the medicinal plants. Manufacturers of herbal medicines should consider standardization of the products while patrons of herbal medicines need to inform their health-care providers about any herbal products they use to ensure effective and safe care. This is to avoid interaction between herbal and allopathic medicines which could yield adverse reaction.

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