REVIEW ARTICLE

Health Risk Associated by Traditional and Complementary Medicines (T&CM) with Special Reference to Herbal Medicines Either Used Alone or Concomitant with Conventional Pharmaceuticals

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Abstract

Traditional and Complementary Medicines (T&CM) are an integral part of health care having deep cited roots in history for the treatment and prophylaction of various mental and physical diseases and to maintain health in good conditions. Although T&CM includes herbal medicines, acupuncture, yoga, and some other indigenous practices this review is mainly focusing on the safety issues associated with the use of herbal medicines (including herbs, herbal materials, herbal preparations, and finished herbal products) either used alone or combined with conventional pharmaceuticals. The trend of using T&CM is on the rise currently as these products are branded as completely safe and free from any kind of adverse effects. This misperception is wrong because a lot of intrinsic and extrinsic factors are responsible to affect the quality of these drugs resulting in severe health consequences. Misidentification of herbs, overdosing, adulteration, and the presence of environmental contaminants like pesticides, heavy metals, and microbial and fungal contaminants are some issues that account for the risks associated with herbal medicines. Another alarming aspect is the concurrent use of both herbal and conventional medicines resulting in interactions of natural phytochemicals with synthetic constituents of conventional medicines resulting in potentiating or antagonizing the pharmacological effects of drugs. The need for time to ensure the quality, safety, and efficacy of T&CM according to the standards of the World Health Organization to make rational use of herbal medicines safe and sound.

Keywords: *Complementary and alternative medicines (CAM), Herb toxicity, Herb-Drug interaction, quality control, Herbal formulation, safety, medicinal plant, concurrent use.*

INTRODUCTION

Drugs originated from nature enjoy great value since prehistoric times but a marked increase in the international trade and commerce in the field of herbs and related products provides great evidence of their worldwide popularity. As per World Health Organization Global Centre for Traditional Medicines (GCTM) 88% of the world's population belonging to both developed and developing countries still rely on the traditional system of medicine. Moreover one hundred seventy member states of WHO report the use of traditional medicines and requested WHO for evidence-based data collection that will guide for setting reforms, policy-making, and regulation of T&CM all over the globe. International Regulatory Cooperation for Herbal Medicines (IRCH) has also become part of WHO in this regard to achieve these goals [1]. According to the WHO Global Report on Traditional and Complementary published in 2019, countries that integrate both T&CM and Conventional Pharmaceuticals in the best way may better meet the unique health challenges of the current scenario [2].

Conventional Pharmaceuticals are medicinal drugs that are the mainstream part of the conventional health care system and are also known as conventional medicines, allopathic and western medicines. On the other hand, Traditional Medicines TM (also known as Non-conventional medicines and un-conventional medicines), Complementary medicines (CM), and Alternative medicines (AM) include health care practices (yoga, acupuncture, mind-body intervention, *etc.*) incorporating herbal medicines obtained from plant, animal, microbe, marine and mineral sources for maintaining physical and mental health [2, 3]. World Health Organization published "WHO traditional medicine strategy 2014-2023" in 2013 where it defined Traditional and Complementary Medicines as "T&CM merges the term TM and CM, encompassing products, practices, and practitioners" [3]. To assure the quality, safety, and efficacy of T&CM all over the globe this document covers all three basic pillars of the healthcare system *i.e.* Products, Practices, and Practitioners [3].

The health care system in Pakistan is comprised of both conventional and traditional systems of medicine. Herbal medicines are a major part of pharmacotherapy in various Traditional settings in Pakistan including Tibb-e-Unani, Homeopathy, Ayurvedic, *etc.* Despite its popularity, most of the Pakistani population is unaware of the potential health risks that may be associated with T&CM [4-7]. The objective of this review is to highlight and discuss the health issues related to the use of T&CM focusing on Herbal medicines either taken as the sole agent or

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combined with conventional pharmaceuticals. This will impart knowledge and awareness not only for general physicians, pharmacists, and medical students but also for practitioners of the traditional system of medicines to use herbal medicines with caution.

METHODOLOGY

An electronic literature search using different databases like Pub Med, Web of Sciences, and Google Scholar was conducted to identify articles related to the risk associated with the use of traditional medicines. Search terms were constructed using terms like herbal medicines, traditional medicines, non-conventional medicines, complementary and alternative medicines, risks, safety, herb-drug interactions, herb-herb interactions, and concurrent use of herb and conventional medicines. Moreover relevant bibliography was hand searched also in this regard. No restrictions were employed regarding the time and origin of publication.

Health Risk Associated with Traditional and Complementary Medicines (T&CM)

There are many reasons why people are moving back towards Traditional and Complementary medicines. Apart from all grounds, one of the main reasons for the popularity of herbal medicines is the misperception that these drugs are completely safe and free from any kind of side effects as happened in the case of conventional allopathic medicines [8-13].

However, the majority of clientele are unaware of the possible health risks related to these natural medicines so consider these drugs completely safe for consumption. This ideology is misleading regarding the safe and effective use of T&CM. It is scientifically proven that quality comprised herbal medicines as well as concurrent use of both allopathic and herbal medicines may lead to severe complications and aggravated disease conditions. A lot of challenges are described by World Health Organization's 2005 global survey report regarding safety and toxicity, quality control, and regulatory status [14-18].

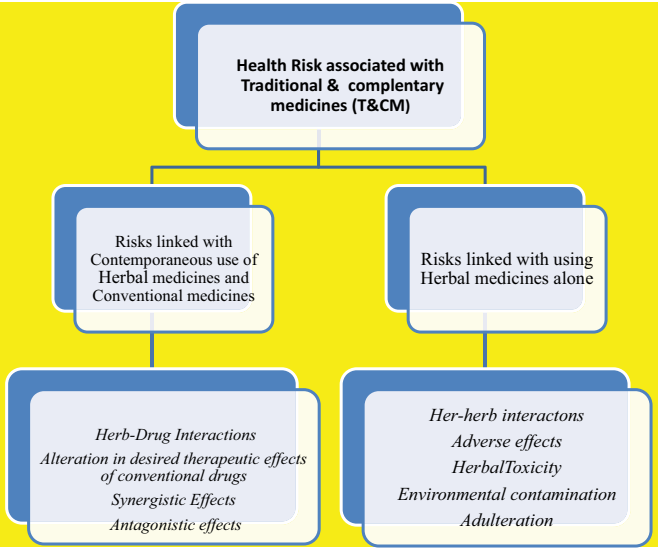

Fig. (1): Potssible Health risks associated with Herbal Medicines.

The use of T&CM especially herbal medicines is not risk-free, but the nature of health hazards depends upon the way these medicines are being utilized. People mostly self-administer different herbs as home remedies or take OTC herbal formulations without any supervision. Another way of utilizing T&CM is to take them as per the prescription recommended by any practitioner of traditional medicine like hakims, homeopaths, Ayurvedic vaid, *etc.* The third common practice is noticed as Co uses of both T&CM and Conventional pharmaceuticals that increase the chances of severe health consequences manyfold. Fig. **(1)** represents a summary of types of health risks that may be encountered using T&CM alone or combined with Conventional medicines.

Risks Linked with Contemporaneous Use of Herbal Medicines/ T&CM and Conventional Pharmaceuticals

It is evident from the scientific literature that majority of the people consider no harm in taking both conventional and unconventional medicines together as they are unaware of the fact regarding interactions between herbs and drugs [19-24]. This malpractice is usually followed to treat some highly prevalent diseases like gastrointestinal (indigestion, acidity, gastritis, constipation, diarrhea, vomiting), respiratory (cough and cold, rhinitis, asthma), urinary tract diseases, skin ailments, weight loss, hypertension, diabetes, *etc.*

Most of the co-users don't inform their healthcare practitioners regarding this practice of simultaneous usage of herbal medicines with allopathic medicines. It may complicate the picture rendering the identification of the true cause of damage.

Herb-Drug Interaction (HDI)

The clinical therapeutic efficacy of conventional drugs is affected by the co-use of herbs and even some food due to the pharmacokinetics and sometimes pharmacodynamic characteristics of drugs. Changes in drug pharmacology due to herb-drug interactions can be explained as the therapeutic effect of any drug being produced due to its active ingredients. Herbal medicines contain biosynthetic phytochemicals like alkaloids, glycosides, phenols, flavonoids, tannins, steroids, *etc.* as the active ingredient, while in the case of conventional medicines active ingredients are synthetic analogues. Interactions between these natural and synthetic compounds are the reason behind herb-drug interactions leading to altered bioavailability of the drug.

Alterations in Desired Therapeutic Effects of Conventional Pharmaceuticals

Sometimes herb-drug interactions will potentiate the therapeutic effects and sometimes they will antagonize the effects. This is a very alarming situation because it may change the pharmacological actions of the drugs. Both pharmacokinetic parameters (Absorption,

distribution, metabolism, and elimination) as well as pharmacodynamic properties of the drug may be altered. To manage the desired bioavailability of the drug dosing protocol should be revised or it is better to avoid such combinations.

Synergistic Effects

Some clinically important HDIs causing the potentisation of conventional medicines are [25-28, 52];

- Garlic (Allium sativum) and Ginkgo (Ginko bibola) potentiate the effects of warfarin resulting in increased bleeding
- Ginko raised blood pressure when combined with thiazide diuretics
- Licorice (Glycyrrhiza glabra) potentiates the effects of oral corticosteroids
- Bitter melon (Momordica charantla) causes less glycosuria when combined with chlorpropamide.

Antagonistic Effects

Some documented HDIs suppressing the effects of conventional medicines are;

- St Jhon wort (Hypericum perforatum) decreases blood levels of amitriptyline, statin, and theophylline digoxin, causes intermenstrual bleeding when used with oral contraceptives, delirium, and mild serotonin syndrome when used with selective serotonin reuptake inhibitors (SSRIs)
- Senna and Cascara may decrease the absorption of certain drugs [25-28, 52].

Risks Associated with Using Herbal Medicines/ T&CM alone

There are a lot of intrinsic and extrinsic factors that result in quality compromised herbal medicines affecting the safety of herbal medicines summarized in Fig. **(2)**.

Herb-Herb Interaction

Interactions between phytochemical constituents of different herbs can also cause problems. This issue is more obvious in the case of polyherbal formulations [29-31].

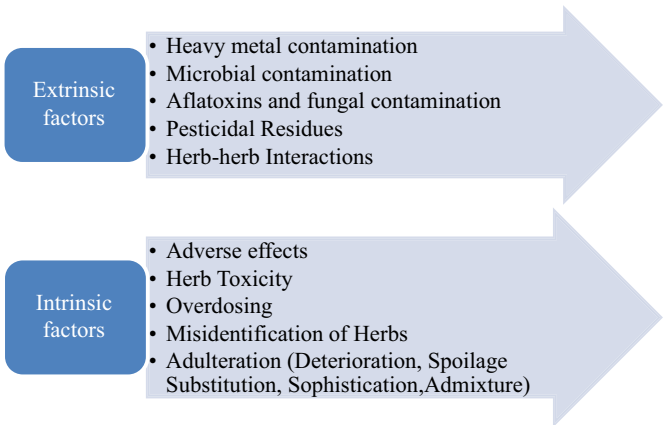

Fig. (2): Factors responsible for affecting the safety of Herbal Medicines.

This can be controlled by complete research on every herb include in the composition of the polyherbal formulation for interactions.

Adverse Drug Events (ADE)

According to the literature, many adverse events are related to the use of herbs including encephalopathy, cardiac issues, bradycardia, respiratory problems, kidney and liver failure, *etc.* [32-37]. These unwanted effects are generally chronic and slowly damage the organs and systems of the human body, so these are not easily traceable. Most adverse events are observed due to poor quality and misuse of T&CM. According to WHO any suspected adverse report should be reported by health professionals [54].

Over Dosing

Herbal formulations are required to be given in appropriate amounts depending on the patient's condition. Taking the wrong amount of herbs as well as the wrong time of their intake may cause harmful effects. Chances of herb overdosing increase due to a lack of supervision and advice from an expert. T&CM should be used following a proper dosage regimen and course of treatment to control dosing frequency, intervals as well as the duration of therapy [38].

Heavy Metal Contamination

Due to environmental pollution medicinal plants and herbal medicines are contaminated with heavy metals. Prevalence of Toxic heavy metals contamination (Pb, Cd, As, Hg) has been documented in herbal drugs. If the rate of metal intake is greater than its clearance, then a gradual buildup of these toxic metals occurs in the body leading to severe organ damage [39-44]. The Agency for Toxic Substances and Drug Registry (ATSDR) have included heavy metals as potentially toxic to human health [45, 46]. United States Pharmacopeia (USP) has issued specific allowable limits of heavy metals in drugs and drug substrates of natural origin for the safe consumption of herbal Medicines [47].

Qualitative and quantitative analysis of heavy metal contents of starting material for herbal medicines must be done before manufacturing as well as in herbal formulations to avoid the accumulation of metals in the body.

Pesticide Residues

To increase the yield of medicinal plants and to prevent them from deterioration and spoilage use of Pesticides is a common practice. These are biocides and their traces in herbs and herbal formulations are a dreadful serious matter [48-51]. All raw materials of herbal medicines must be checked for the presence of pesticide residues.

RECOMMENDATIONS AND SUGGESTIONS

To ensure the quality, efficacy, and safety of herbal medicines guidelines are provided by several health-related international agencies and organizations like

World Health Organization (WHO) [1-3, 54], European Medicines Agency (EMA) [53], the United States Pharmacopoeia Herbal Medicine compendium (HMC) [55], American Herbal Product Association- American Herbal Pharmacopoeia(AHPA-AHP) [57], *etc.* It is suggested that all guidelines and strategies must be followed to regulate the products, practices, and practitioners of T&CM.

To control Contaminants and residues in herbal medicines WHO has published guidelines [18] that should be consulted. USP also provides allowable limits for heavy metals testing in herbal medicines [42].

To ensure the safety of herbal medicines WHO has issued guidelines relating to the Pharmacovigilance of herbal medicines [54, 56].

Medicinal plants are the starting materials of herbal medicines. WHO and USP HMC has published monographs on different medicinal plants that must be referred to for the standardization of herbal medicines. Moreover WHO, AHPA-AHP also provides guidelines for the preparation of herbal medicines from medicinal plants according to scientific standards. [57-59].

For research and development related to traditional medicines, WHO guidelines should be referred to [60].

CONCLUSION

The importance of T&CM can never be avoided especially in herbal medicines as these are not only the basic search engine for new conventional Pharmaceuticals but also utilized as therapeutic agents in traditional systems of medicine. Moreover, it is a common practice to co-use both T&CM and Conventional Pharmaceuticals in many disease conditions. Due to the rapid expansion of global demand for herbal drugs, it is the need of time to pay attention to the Pharmacovigilance and quality control of non-conventional to safeguard their effects and control the risks associated with their use. Awareness should be done to the general public, physicians, pharmacists, and traditional practitioners regarding the toxicity and adverse reactions of traditional medicines. Especially attention should be paid to spreading the knowledge about the consequence of herb-drug interactions and concurrent use of both medicines should be discouraged without supervision.

ABBREVIATIONS AND ACRONYMS

ADR Adverse Drug Reaction
AHP American Herbal Pharmacopoeia
AHPA American Herbal Product Association
ATSDR Agency of Toxic Substances and Drug Registry
CAM Complementary and Alternative Medicines
CM Complementary Medicines
EMA European Medicines Agency
HDI Herb-Drug Interactions
HMC Herbal Medicine Compendium
OTC Over the Counter
T&CM Traditional and Complementary Medicines
TM Traditional Medicines
USP United States Pharmacopoeia
WHO World Health Organization

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None.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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