

Navigating ethical dilemmas in complementary and alternative medicine: a narrative review

Mohammad Sadegh Adel Mehraban¹, Asieh Mosallanejad², Mehdi Mohammadi³, Ozra Tabatabaei Malazy^{4*}, Bagher Larijani^{5*}

1. PhD Candidate of Traditional Medicine, Department of Traditional Medicine, School of Persian Medicine, Tehran University of Medical Sciences, Tehran, Iran; Traditional Persian Medicine and Complementary Medicine, Student Association, Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran.

2. Assistant Professor, Department of Pediatric Endocrinology & Metabolism, Imam Hossein Medical Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

3. Assistant Professor, Department of Clinical Pharmacy, School of Pharmacy, Alborz University of Medical Sciences, Karaj, Iran.

4. Associate Professor, Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran; Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

5. Professor, Medical Ethics and History of Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran of Medical Sciences, Tehran, Iran.

Abstract

Complementary and alternative medicine (CAM) is a rapidly growing industry, with millions worldwide seeking these treatments for various ailments. While many CAM therapies have shown promise in improving health outcomes, there are also ethical challenges associated with them. In this article, we explore some of the most pressing ethical issues in CAM, including informed consent, justice in accessibility, and evidence-based therapies. This survey provides a comprehensive overview of the ethical issues in CAM and offers practical guidance for health-care providers navigating these complex issues. By understanding the ethical dilemmas in CAM, health-care providers can offer their patients safe and effective care while maintaining their professional and ethical obligations.

*Corresponding Author

Ozra Tabatabaei Malazy*

Address: Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Postal Code: 14 11 71 31 35

Tel: (+98) 21 88 22 00 38

Email: tabatabaeiml@sina.tums.ac.ir

Bagher Larijani*

Address:

No:23, 16 Azar St., Medical Ethics and History of Medicine Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Postal Code: 1417633114

Tel: (+98) 21 66 41 96 61

Email: emrc@tums.ac.ir

Received: 8 Oct 2023

Accepted: 17 Jan 2024

Published: 27 Apr 2024

Citation to this article:

Adel Mehraban MS, Mosallanejad A, Mohammadi M, Tabatabaei Malazy O, Larijani B. Navigating ethical dilemmas in complementary and alternative medicine: a narrative review. *J Med Ethics Hist Med.* 2024; 17: 3.

Keywords: Complementary medicine; Persian medicine; Alternative medicine; Ethics.

Introduction

Complementary and alternative medicine (CAM) is defined as “a group of diverse medical and health-care systems, practices and products that are not presently considered to be part of conventional medicine” (1).

An increasing trend in using and searching for CAM by people and scientists is currently reported in both developed and developing countries (2 - 5). In the UK, several studies suggest that up to 66% support CAM in the National Health Service. In Norway, 43 - 63% believe CAM should be available for hospital cancer patients. In Germany and Switzerland, where GPs often provide CAM, up to 70% in primary care opt for these treatments (6). Reported reasons include avoiding the side effects of conventional treatments, positive aspects associated with herbal medicine, past good experiences, and the lower cost of CAM compared to conventional treatments. In addition to their appeal as traditional or complementary treatments, herbal medicines remain a cornerstone in the advancement and exploration of novel drug development (7, 8).

More nations have been recognizing the need for a unified health-care approach that will benefit governments, professionals and individuals. This

enables secure, respectful, cost-effective access to CAM while ensuring its efficacy (9). Although some CAM therapies hold scientific validation, crucial inquiries remain unresolved, demanding rigorous and carefully designed scientific investigations. In spite of the popularity of CAM and its contribution to the pharmacopeia, three core questions persist, involving the safety of these therapies and their effectiveness in addressing the diseases or medical conditions for which they are recommended (1). There are indications that a significant portion of herbal medicines are introduced to the market to gain popularity for usage without undergoing the standard scientific developmental phases (10). This can be attributed to factors such as statistical analysis, biases in risk assessment, and researchers' limited knowledge (10). Moreover, CAM physicians encounter major ethical challenges in clinical practice in three areas: professionalism, professional communications, and regulations and policies (11). Given the aforementioned points about CAM and herbal medicine, it is vital to consider the ethical challenges, and while the release of herbal medicines to the pharmacopoeia should not be prevented, customers should be aware of the

potential benefits and harms. Hence, the aim of this review is to investigate ethical considerations about CAM in research and clinic.

Methods

All original and review articles on PubMed, Web of Science and Scopus web databases were searched using the following keywords: ethics, complementary medicine, Persian medicine, and alternative medicine. After excluding duplicated articles and un-related studies, relevant studies were retained and summarized.

Results

Ethical Issues

There are numerous ethical challenges in the field of CAM, some of which are as follows:

1) Natural Products in Evidence-Based Literature

Natural products, like plant extracts, often exhibit intricate pharmacological profiles that can have various physiological outcomes, manifested as advantageous synergies or potentially detrimental interactions, depending on the context in which they are applied (12,13). In Germany, CAM can be legally administered by non-medical practitioners. This situation might lead patients to perceive CAM as a benign form of treatment. Patients are often presented with the notion that CAM treatment methods are completely devoid of adverse effects.

Using medical terms informally like ‘natural medicine’ or ‘experience-based medicine’, which are not scientific, fosters the belief that CAM is a mild and secure approach to healthcare (14). Patients who undergo treatments with CAM approaches report “less severe adverse effects” as one of the most prevalent reasons for visiting a CAM practitioner (15).

2) Justice in CAM: Accessibility

Throughout Europe, a significant portion of the population bears personal expenses for CAM. Studies reveal that CAM use is favored by well-educated, working-age individuals with higher incomes. However, the financial landscape associated with CAM varies across Europe. Whether only the affluent can afford CAM or the less privileged can access it due to its relative affordability, CAM’s financial aspects illuminate health-care disparities. These dimensions’ underscore health-care system inequities, exacerbating pre-existing health inequalities (6). The unequal distribution of CAM is solemnly opposite to fundamental ethical principles. Also, CAM has evolved into a lucrative unregulated sector within the United States, encompassing a multibillion-dollar industry. The financial burden of CAM falls almost entirely upon consumers, who

concurrently bear the potential hazards of utilizing these therapies without adequate supervision (16).

3) Patients' Unawareness of Certain CAM Therapies

Even though patients frequently turn to CAM, there usually exists a need for more communication and shared comprehension of CAM between patients and their medical practitioners. In certain instances, patients may lack knowledge of specific beneficial treatments and seek advice from unsupervised CAM practitioners, which can have serious repercussions (17). Patients might opt for herbal remedies to alleviate various symptoms, yet these products could also contain constituent chemicals with unexplored intrinsic effects or unintended side effects owing to potential contaminants (18). Clinicians should inquire about patients' use of CAM because it is vital to address quality of life, symptoms and lifestyle alongside conventional treatments. Research strategic plans should feature well-designed clinical studies assessing CAM, validating through evidence its effects on survival, symptoms and well-being (17).

4) Unknown Plant Components and the Quality of Herbs

With the global surge in herbal medicine use and the rapid international market expansion, ensuring safety and quality of herbal ingredients and products is a growing concern for health regulators,

pharmaceutical firms and the general public. The efficacy of herbal medicines hinges on their quality, and quality control of finalized herbal products, especially blends, is more complex than chemical drugs. A product's excellence is clearly tied to the quality of the raw materials used (19). In the pharmaceutical industry, patentability of natural medicinal products is an important factor for investment in funding research related to CAM. Moreover, the execution of meticulously planned CAM studies incurs significant expenses (20).

5) Methodological Issues: Interactions, Safety, and Efficacy in Research

Research into CAM entails unique challenges in terms of methodology. This is primarily because assessing personalized and holistic CAM approaches often necessitates application of more distinct criteria compared to those traditionally employed for evaluating conventional medical interventions (21). Although herbal treatments are potent and sometimes toxic and there are well-known interactions (herb-drug and herb-herb), there is not enough scientific data on the safety of herbal products (21, 22).

A current area of focus pertains to examining interactions between drugs and herbs, encompassing absorption, distribution, metabolism and excretion (ADME) of medications. An

encouraging prospect of aligning with the existing FDA and EMA guidelines exists for assessing herbal medicines in the context of drug-drug interactions (DDI) (23).

Like synthetic drugs, CAM therapies should meet evidence-based criteria. This involves crafting a scientifically rigorous proposal with defined inclusion/exclusion criteria, informed consent protocols, and approval of ethics committees. Ideally, a well-designed phase II or III trial is crucial to validate expert opinions. Herbal medicine safety and efficacy are vital, especially in developing regions with widespread usage. The significance of herbal medicine use cannot be understated. The World Health Organization (WHO) reported that a substantial portion of the population, approximately 80% in Africa and 70% in India, rely on herbal remedies for addressing various ailments (24). Due to safety concerns in herbal remedies, regulatory bodies must implement measures to protect public health, and this involves stringent safety and quality standards for all herbal medicines (25).

A fundamental requirement lies in conducting comprehensive safety assessments for both herbal and conventional drugs, especially when the potential for co-administration exists. Many methodologies utilized in formulation and

assessment of conventional pharmaceuticals can be tailored to suit plant-derived medications. These evaluations would contribute remarkable value to herbal treatments, as health-care practitioners and patients better accept drug and herbal medicine usage. Additionally, this process could foster the establishment of instructions endorsed by regulatory organizations such as Food and Drug Administration (FDA) and government agencies overseeing medicinal usage (23).

While treatments involving these agents show promise, many herbal products still need to be tested using adequate monitoring because of gaps in understanding their mechanisms, adverse effects, pharmaceutical interactions and safety alongside functional foods. For the time being, our limited knowledge of these issues hampers safe and rational use.

Discussion

Solutions to the ethical issues in CAM research and studies

Advocates of Complementary and Alternative Medicine (CAM) often emphasize its holistic approach and suggest that certain therapeutic advantages might operate on levels that are not easily captured through quantitative assessments. On the contrary, evidence-based medicine heavily relies on outcomes that are reproducible and

quantifiable. This dynamic could introduce an ethically concerning bias within conventional medicine, possibly sidelining areas of healthcare where outcomes are not easily quantified or precisely defined (26). Numerous CAM therapies are rooted in philosophical frameworks that diverge from conventional medical viewpoints, hindering their scientific validation through traditional methods. Nevertheless, it is evident that these philosophical disparities only partially impede the potential for robust and effective CAM research (26). The following recommendations can be helpful in practicing CAM safely and effectively:

1) Extensive Research into Herbal Treatments

When exploring the quality, potential effects, safety and molecular assessments of commonly used plants, extensive research seems to be crucial. Fortunately, modern scientific progress equips us with tools for these inquiries. Innovations like genomic/proteomic testing and chemical fingerprinting, aided by advanced testing platforms, authenticate and ensure herbal product quality. Therefore, regulations should enforce these techniques to ensure consumer protection (27).

2) Defining Herb Quality Criteria

The integration of herbal medicines into drug regulations was initially recognized during the WHO International Conference on Drug Regulatory Authorities in 1986 (28). Following this, in 1991, the World Health Organization developed initial guidelines for the assessment of herbal medicines (29). These guidelines incorporate crucial criteria pertaining to the quality, safety and efficacy of herbal medicines. In ensuring the safety, efficacy, standardization and documentation of herbal medicines, which are integral to various CAM practices, several critical criteria are employed. Firstly, authentication involves the meticulous identification of plant species using their Latin binomial names, coupled with detailed taxonomic, macroscopic and microscopic studies. Physical parameters are rigorously assessed, including sensory characteristics, viscosity, moisture content, pH and other physical aspects, supported by advanced analytical techniques like UV-visible spectrophotometry and HPLC for evaluating active constituents. Microbiological analysis is crucial, focusing on the detection and quantification of contaminants like *E. coli*, molds and aflatoxins and adherence to established pharmacopeial standards. Pesticide residue analysis is also conducted, ensuring levels of harmful substances like DDT

and BHC are within WHO and FAO prescribed limits. Lastly, heavy metal analysis is performed, testing for toxic metals such as lead, mercury and arsenic, with a particular emphasis on metal speciation. Collectively, these criteria are pivotal in guaranteeing the quality and safety of herbal products and can be adapted to suit a range of CAM modalities, underscoring a commitment to quality control and consumer safety. To sum up, these guidelines hold immense value as resources, aiding national regulatory bodies, scientific organizations and manufacturers in their endeavors to comprehend and uphold these standards (30).

3) Adopting a Scientific Approach to CAM

In medicine, showcasing intervention efficacy is insufficient, but unveiling underlying mechanisms is crucial. Although science starts with observation, definitive evidence and details are required. This assertion remains valid for both herbal products and conventional therapies. Despite varying health outcomes, the approach to gathering evidence on effectiveness stays fundamentally consistent (31). Implementing a standardized approach for herbal practitioners and collecting prospective data establishes an intervention framework that, when properly structured, closely resembles single-blind randomized trials. It is worth highlighting that a notable increase in the successful execution and

documentation of randomized clinical trials focused on herbal medicines has been observed in recent years (30).

CAM researchers must be attentive to the socio-cultural aspects of diseases, interactions between practitioners and patients, and adherence to treatments. Research in this field encompasses a range of approaches, including empirical, semi-empirical and descriptive, as well as case presentations and historical interviews. Factors such as regional variations, patient-centric perspectives, integration of methods, participant selection criteria and the choice of placebos can significantly influence research outcomes (32).

Practitioners can embody care, respect, honesty and fairness in practice. Reflecting on these values reveals ethical lapses. In education, a values-based approach highlights areas where educators can improve ethics. Understanding herbal medications is one facet of ethical care's multifaceted demands (7).

It is crucial for CAM practitioners to comprehend conventional medical practices (COM) through education; likewise, it is valuable for conventional physicians to grasp CAM, including its terminology, diagnostics and treatments. As CAM's prevalence grows, its integration into academic curricula becomes more beneficial,

fostering a comprehensive health-care approach among future professionals (21). The establishment of numerous peer-reviewed journals focused on CAM has the potential to promote the advancement of research discussions. Additionally, this can simplify the process of validating the qualifications of individual practitioners (21). Guidelines for manufacturing, quality control and therapeutic application, encompassing details like indications, dosages, side effects and potential safety considerations, are frequently offered by governments, the World Health Organization (WHO) and panels comprising academic experts and medical practitioners. A significant portion of these directives is consolidated within pharmacopeial monographs (30).

4) Plant Toxicity Evaluation

To evaluate the potential toxic effects of plant constituents within herbal formulations, thorough phytochemical and pharmacological investigations are of the essence. Potential herbal preparation toxicity arises from inherent plant constituent toxicity and manufacturing irregularities or contaminations. The Committee for Proprietary Medicinal Products (CPMP) guidelines emphasize stringent control over raw materials and final products. These guidelines highlight the

importance of Good Manufacturing Practices for product integrity and safety (33).

5) Using Standardized Herbal Products

To conduct reliable clinical trials and ensure consistent therapeutic benefits, it is imperative to have standardized herbal products that exhibit uniform quality and well-defined constituents. Reliable clinical outcomes can only be expected when a phytochemical mixture maintains consistent quality. The renewed interest and expanding market for herbal medicinal products underscore the importance of a collective commitment by all parties to safeguard consumers and the industry.

Standardization plays a foundational role in establishing uniform biological activity, a consistent chemical profile and a robust quality assurance system for the process of production and manufacturing. This critical step is vital in ensuring the reliability and effectiveness of herbal products within the realm of healthcare (30).

6) Prescription by an Expert or Educated Physician in the Field

Physicians can access reliable databases detailing herbal benefits and potential side effects, including drug-herb interactions. National conventions offer courses, workshops and training for health-care professionals to integrate complementary therapies

(16). Ethics educational programs with intrinsic motivations for practical ethics offered to medical professionals can cover some clinical challenges, especially for medicine and pharmacy students (34 - 36). Medical schools and academic health centers offer CAM education, integrating complementary therapies into curricula. In clinical case studies, health-care students study complementary therapies alongside conventional treatments, which will prepare them for a broad spectrum of therapies (17). In situations where uncertainties surrounding effectiveness and safety arise, particularly with numerous natural products, transparent communication should convey to patients the uncertainty level of the treatment's effectiveness and safety.

Additionally, patients should be made aware of alternative treatment options, their availability and the balance between risks and benefits. Presenting this information to patients will help them to better comprehend the inherent uncertainties and subsequently make informed decisions about whether to accept or decline treatments involving natural products (37). The guiding principle for physicians should revolve around the evaluation of patient safety and the effectiveness of natural products (38).

7) Patients' Freedom of Choice

As long as patients have the freedom to decide on their treatment without coercion, no ethical objections exist to the utilization of CAM as a form of practice. It is important to note that CAM as a belief system cannot be justified by this principle, as it pertains to decision-making rather than belief adoption. Given that certain CAM approaches encompass robust spiritual convictions, an individual may opt for a CAM therapy based on personal choice, even if its effectiveness is questioned (39). In the realm of CAM, autonomy is extended even to the 'spiritual level'. A practitioner has the potential to attain spiritual consent at the subconscious level, which is considered to be equally or possibly more significant than conscious consent (40). CAM tends to lean more toward a paternalistic approach compared to biomedicine. In CAM the patient, often referred to as a 'client', holds the practitioner in high regard as a 'knowledgeable individual' endowed with the capacity to mediate with deities and spirits in order to facilitate the process of healing. This emphasis on the practitioner's character is related to the central role of spirituality in healing (40). The principle of beneficence can be employed to support the rationale for CAM. If there exists an ethical duty to make every effort to enhance a patient's well-being, and CAM presents itself as a

means to achieve this goal (or potentially an even more effective approach), then justifying the practice of CAM is warranted (39). The central ethical tenets of CAM encompass a reverence for autonomy, the principle of beneficence, and the safeguarding of freedom of speech, thought and religious beliefs. While collisions between these principles and the concept of non-maleficence and considerations pertaining to informed consent have been evidenced as probable, the principle of justice may also positively influence CAM practices.

Furthermore, a range of shared and unique values have been recognized between conventional biomedicine and CAM (39). Many individuals highly appreciate the patient-centered approach and holistic principles that are integral to numerous CAM consultations. They have a high regard for the positive relationship between CAM providers and patients, characterized by mutual respect and understanding. Moreover, the explanatory models regarding health and illness often align closely with the personal beliefs and perspectives of these individuals (6).

8) Taking into Account Ethical Frameworks and Considerations

Health-care practitioners commonly operate within a framework guided by ethical principles, that is, beneficence, nonmaleficence, autonomy and

justice. These principles collectively dictate that health-care professionals should strive to promote well-being, prevent harm, honor individuals' right to self-determination and ensure equitable treatment for all individuals (41).

Because herbal medicine production and utilization is performed worldwide, our suggestion is to employ a universal ethical structure. Chatfield and colleagues express a preference for a values-centric rather than a principles-centric framework. Specifically, they advocate embracing values such as *care, respect, honesty* and *fairness* (7).

Expressing care in the realm of herbal medicine involves demonstrating genuine concern for the well-being of both the individuals who rely on these remedies and the broader communities and ecosystems that provide the sources for these treatments (7). Respect entails recognizing that individuals may have preferences, traditions and cultural contexts different from one's own. In the realm of healthcare, it signifies that a health-care provider acknowledges and supports a treatment approach or decision even if it does not align with their personal choices. The principle of 'honesty' serves as a fundamental cornerstone for ethical human interaction across all societies and countries. Nevertheless, within healthcare, the notion of honesty assumes a more expansive and

crucial role. While purposeful falsehoods are evidently unethical, it is equally improper to withhold crucial information essential for obtaining informed consent. As a result, honesty demands that herbal practitioners transparently communicate the available evidence related to the effectiveness and potential risks of their treatments. The fairness principle in herbal medicine encompasses various interpretations. For instance, fairness in distribution ensures that treatments are widely available and accessible to all, promoting equal health-care opportunities. Corrective fairness, on the other hand, involves compensating for erroneous medical decisions, emphasizing accountability and responsibility in the health-care process. Finally, fairness in exchange pertains to equitable service charges, emphasizing the ethical consideration of fair and just financial transactions within the herbal medicine domain (7).

9) Establishing Specialized Ethical Frameworks for CAM

The previously outlined ethical framework has been fine-tuned to better accommodate international research, providing a practical foundation for addressing ethical considerations in the realm of global traditional herbal medicine studies. New components include: 1) Collaborative partnership: In collaborative partnerships, it is

important for the leadership in research to equally represent and respect both sides. This means listening to and including advice from the community involved. Also, there is a focus on providing training and building skills in science, especially in countries where these resources are not as developed. This helps in creating long-lasting research projects in these countries and ensures that everyone involved is on an equal footing; 2) Social value: Insights derived from the research ought to possess the capacity to pave the way for novel, widely applicable knowledge or enhancements in healthcare; 3) Scientific validity: The design of research should be oriented toward generating advantageous and universally applicable knowledge; 4) Fair subject selection: The selection of subjects should be guided by scientific significance, rather than convenience, susceptibility or prejudice; 5) Favorable risk-benefit ratio: Individual engagement should offer potential advantages that surpass the associated participation risks; 6) Independent review: Preserving research integrity requires independent bodies, separate from the investigators, to concur that the risks and potential benefits associated with the research are warranted; 7) Respect for subjects: Participants should be aware of their right to withdraw from the study. Additionally, there

should be a system in place to monitor the research for any pertinent adverse events; and 8) Informed consent: Researchers must secure valid consent for study participation from subjects (42 - 44).

Conclusion

It seems there is a gap between scientists, physicians, manufactures and ethicists in knowledge, practice and attitude related to CAM use in research and clinical medicine. Therefore, we propose the establishment of a framework that

involves a strong collaboration among researchers, physicians, manufacturers and ethicists. This collaborative effort would formulate a cohesive strategy aimed at elevating ethical standards within the domain of CAM research and clinical practice.

Acknowledgements and funding

The study did not receive any funding.

Conflict of Interests

There are no competing interests to declare.

References:

1. Wai Fan K. National center for complementary and alternative medicine website. *Journal of the Medical Library Association*. 2005; 93(3): 410.
2. Tabatabaei Malazy O, et al. Quality of reporting of randomized controlled trials of herbal medicines conducted in metabolic disorders in Middle East countries: a systematic review. *Complement Ther Med*. 2018; 38: 61-6.
3. Tabatabaei Malazy O, Larijani B, and Abdollahi M. Targeting metabolic disorders by natural products. *Journal of Diabetes & Metabolic Disorders*. 2015; 14: 1-21.
4. Tabatabaei Malazy O, et al. New horizons in treatment of osteoporosis. *DARU Journal of Pharmaceutical Sciences*. 2017; 25: 1-16.
5. Moeini R, et al. The prevalence of complementary and alternative medicine use in the general population of Babol, North of Iran, 2018. *BMC Complement Med Ther*. 2021; 21(1): 113.
6. Nissen N, et al. Public health ethics for complementary and alternative medicine. *European Journal of Integrative Medicine*. 2013; 5(1): 62-67.
7. Chatfield K, et al. Applying an ethical framework to herbal medicine. *Evidence-based Complementary and Alternative Medicine*. 2018; 2018.

8. Welz AN, Emberger Klein A, Menrad K. Why people use herbal medicine: insights from a focus-group study in Germany. *BMC Complementary and Alternative Medicine*. 2018; 18: 1-9.
9. Organization WH, WHO traditional medicine strategy: 2014-2023. 2013: World Health Organization.
10. Javadi Pashaki N, et al. Methodological and ethical challenges for the implementation of complementary and alternative medicine-related clinical trials: review of reviews. *Jorjani Biomedicine Journal*. 2022; 10(3): 61-9.
11. Esmalipour R, Larijani B, Mehrdad N, Ebadi A, Salari P. The ethical challenges in pharmacy practice in community Pharmacies: a qualitative study. *Saudi Pharm J*. 2021;29(12):1441- 8.
12. White A, et al. Reducing the risk of complementary and alternative medicine (CAM): challenges and priorities. *European Journal of Integrative Medicine*. 2014; 6(4): 404- 8.
13. Pai Vasudev, et al. "Issues and challenges in pharmacovigilance of Herbal formulations." *Current Drug Safety*. 2024: 19-23.
14. Baatsch B, et al. Complementary and alternative therapies in dentistry and characteristics of dentists who recommend them. *Complementary therapies in medicine*. 2017; 35: 64-9.
15. Chowdhuri PD, and Kundu K. Factors determining choice of complementary and alternative medicine in acute and chronic diseases. *J Complement Integr Med*. 2020;17(3).
16. Richardson MA, et al. Complementary/alternative medicine use in a comprehensive cancer center and the implications for oncology. *Journal of Clinical Oncology*. 2000; 18(13): 2505-14.
17. Rosenthal DS, Dean Clower E. Integrative medicine in hematology/oncology: benefits, ethical considerations, and controversies. *ASH Education Program Book*. 2005(1): 491-7.
18. Oh W K, et al. Prospective, multicenter, randomized phase II trial of the herbal supplement, PC-SPEs, and diethylstilbestrol in patients with androgen-independent prostate cancer. *Journal of clinical Oncology*. 2004. 22(18): 3705-12.
19. Zhang M, et al. Comparison of the guidelines on good agricultural and collection practices in herbal medicine of the European Union, China, the WHO, and the United States of America. *Pharmacol Res*. 2021; 167: 105533.
20. Gurgula O, Strategic patenting by pharmaceutical companies - should competition law intervene? *IIC Int Rev Ind Prop Copyr Law*. 2020; 51(9):1062-85.

21. Teichfischer P. Ethical implications of the increasing use of complementary and alternative medicine. *Complementary Medicine Research*. 2012; 19(6): 311-8.
22. Werner S M. Patient safety and the widespread use of herbs and supplements. 2014: *Frontiers Media SA*. p. 142.
23. Thelengwani R, Masimirembwa C. Evaluation of herbal medicines: value addition to traditional medicines through metabolism, pharmacokinetic and safety studies. *Current Drug Metabolism*. 2014; 15(10): 942-52.
24. Organization WH, National policy on traditional medicine and regulation of herbal medicines: Report of a WHO global survey. 2005: World Health Organization.
25. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol* 2014; 4: 177.
26. Ernst E, Cohen MH, Stone J. Ethical problems arising in evidence based complementary and alternative medicine. *Journal of Medical Ethics*. 2004; 30(2): 156-9.
27. Benzie IF, Wachtel-Galor S. *Herbal medicine: Biomolecular and Clinical Aspects*. 2011.
28. Organization WH. ICDRA: International conference of drug regulatory authorities (ICDRA) comes to Africa. *WHO Drug Information*. 2016; 30(2): 173-5.
29. ICDRA. 19th International Conference on Drug Regulatory Authorities. 2021, World Health Organization Geneva.
30. Mosihuzzaman M, Choudhary MI. Protocols on safety, efficacy, standardization, and documentation of herbal medicine (IUPAC Technical Report). *Pure and Applied Chemistry*. 2008; 80(10): 2195-2230.
31. Plantadosi S. In *Clinical Trials: A Methodologic Perspective*. New York: John Wiley & Sons, 2017.
32. Omur S. Ethical Evaluation of Clinical Research on Complementary and Alternative Medicine, IN *Bioethics in Medicine and Society*, Thomas FH, Sujoy R, Editors. Croatia: Intech Open, Rijeka. Ch. 7.
33. Communities C. *The Rules Governing Medicinal Products in the European Community: Guidelines on the quality, safety, and efficacy of medicinal products for human use*. Office for Official Publications of the European Communities. 1989; Vol. 3.
34. Mashayekhi J, Mafinejad MK, Changiz T, Moosapour H, Salari P, Nedjat S, Larijani B. Exploring medical ethics' implementation challenges: a qualitative study. *J Educ Health Promot*. 2021; 10:66.

35. Madani M, Ghasemzadeh N, Dizani A, Gharamaleki AF, Larijani B. Policy considerations to achieve practical ethics: closing the gap between ethical theory and practice. *J Med Ethics Hist Med.* 2020; 13:8.
36. Salari P, Abdollahi M. Ethics in pharmacy curriculum for undergraduate pharmacy students: a needs assessment study. *Arch Iran Med.* 2017; 20(1): 38-42.
37. Chatfield K. Traditional and complementary medicine: analysing ethical challenges. Diss. University of Central Lancashire. 2016.
38. Di Paolo M, et al. Natural products in neurodegenerative diseases: a great promise but an ethical challenge. *International Journal of Molecular Sciences.* 2019; 20(20): 5170.
39. Seidlein AH, Salloch S. Illness and disease: an empirical-ethical viewpoint. *BMC Med Ethics.* 2019; 20(1): 5.
40. Taylor RM. Ethical principles and concepts in medicine. *Handb Clin Neurol.* 2013; 118: 1-9.
41. Childress JF. Respecting Personal Autonomy in Bioethics: Relational Autonomy as a Corrective? In James F. Childress & Michael Quante (eds.), *Thick Autonomy: Personal Autonomy in Ethics and Bioethics.* Germany: Springer Verlag; 2022. p. 135-49.
42. Emanuel EJ, et al. Ethical issues concerning research in complementary and alternative medicine, in *The Ethical Challenges of Human Research: Selected Essays.* UK: Oxford University Press; 2012.
43. Tilburt JC, Kaptchuk TJ. Herbal medicine research and global health: an ethical analysis. *Bulletin of the World Health Organization.* 2008; 86: 594-9.