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Perspective

Herbs and Herbal Medicine: The Need for Evidence Based Direction

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Abstract

Herbs and herbal substances have been a part of unconventional medical practice since the dawn of medicine, mainly found in folk and traditional applications and deriving from observation, established conventions, experience and spiritual, cultural rituals. Nowadays herbs and plant extracts are the center of attention for westernized industries, scientific clusters and social groups, although the attitude of the majority of scientific community towards this kind of remedies remains negative and skeptical, as there is limited scientific-based knowledge and a scarcity of rigorous conclusions that can be further utilized as official guidelines in conventional medical practice. Thus, it is crucial that herbs and their future use as preventive or therapeutic medicine be the subject of well-designed clinical studies, as the majority of herbs and extracts that have been examined for their effect in the GI system concentrate on IBS and IBD symptoms' management and don't provide conclusive results. Apart from that, this area is a promising and wide research tank from socio economic, nutritional and environmental perspective. To this end, there are many significant aspects that should be taken into consideration such as the quality control of herbal medicine, the structure of clear frameworks and legislations as to their use as medicines, the correct selection of the herbal species that may have additional value among the numerous existing ones, the sustainable exploitation of the plants and the potential side effects that may exist and should be further explored. In a nutshell, all the aforementioned facts elucidate the need for deep and substantial research in this unexplored area, which seems to be promising but lacks of scientific background, research foundation and institutional support.

Keywords: *Herbs; Herbal Medicine; GI Diseases; Scientific Data; Further Research*

Abbreviations

CAM: Complementary and Alternative Medicine; GI: Gastrointestinal Disorders; IBD: Inflammatory Bowel Disease; IBS: Irritable Bowel Syndrome; WEFs: Wild Edible Fruits

Introduction

Herbs and herbal substances have been a part of unconventional medical practice since the dawn of medicine [1]. The foundation of their use to treat or prevent human diseases lies on observation, established conventions, personal experience, past knowledge and other subjective factors that are related to a more arbitrary, cultural, spiritual, ethnic, social and religious basis rather than be acquired from a scientific perspective [2,3]. In other words, the most commonly used herbal supplements and medicine have evolved from folk and traditional applications [1,4-6], mainly in Africa and Asia (such as Traditional Chinese Medicine) [7,8] but nowadays westernized societies are all the more interested in such remedies, as they seek and turn to alternative and natural ways to approach the coveted wellbeing [9,10]. Under this umbrella, herbs, herbal medicine and dietary supplements constitute a specific category of Complementary and Alternative Medicine [2], an abstract term aiming to describe the medical products and practices that are not part of standard medical care, and a definition wide enough to include all alternative services and products that can be regarded as CAM, under educational, socio-economic, cultural and ethnic terms [3]. On the other side of the coin, it is an undeniable fact that the prevailing attitude of the majority of scientific community and medical practitioners is characterized by skepticism about those methods, being mainly reluctant and negative not only

to prescribe such medicine but even to support their potential benefits in theoretical assumptions and controversial debates, elucidating herbs as the new placebo [11]. This attitude can be justified from the scarcity of the scientifically based knowledge as to the relation of their impact on human's health, as well as from the primitive instinct that something so unfamiliar, unknown, groundless and spiritual cannot have worthy practical efficacy.

However, last decades herbs and herbal medicine are the center of attention for industries, scientific clusters [12,13] and social groups [14], mainly because global priorities have changed a lot [3] and they are directed to sustainability, environmental preservation, social equality and empowerment of developing world and people's re-connection with nature and tradition [10]. In parallel, technological breakthroughs enable for new research opportunities and innovation to the health sector, all these contributing to the emergence and exploitation of herbs in many ways, other than the traditional uses [15]. In this context, herbs have many applications in medical practices in general, and more specifically in the digestive system, where their use is by far the most well-known and frequent.

Need for Further Research

As a part of Complementary and Alternative Medicine (CAM), herbs, plant extracts and herbal medicine are the most popular and frequently used category among patients with GI disorders [10,16]. To be more specific, the most recent statistical data reveal that CAM are used by almost 50% of the patients with IBD at least for a short period of time [17] while the use of herbals as treatment of either active or quiescent disease exceeds the proportion of 58% [10]. The same applies to people with IBS, often attempting to self-treat their symptoms with non-prescribed pharmacological regimens and/or complementary and alternative medicines (CAM) [16,18]. Based on the aforementioned, it can be recognized that herbal medicine is rather popular within patients and this conclusion, together with the fact that a growing body of evidence underpin the potential promising utility of specific herbs in GI disorders illustrate once more the need for the establishment of rigorous scientific data. Nonetheless, it goes without saying that due to the limited available scientific knowledge [17,19] most medical practitioners, especially in western societies, are reluctant to implement or prescribe such remedies, and not unjustifiably, as their perceived natural and healthy properties are not sufficient to guarantee effective and safe health outcomes [20].

Available Scientific Data

In general terms, as to the scientific data that examine the association of herbs and herbal medicine with the gastroenterology disorders, the majority of reviews and meta-analyses converge on the fact that there is limited knowledge and a scarcity of research based and high valid conclusions that can be converted into official recommendations and guidelines to be safely and efficiently utilized in conventional medical practice [17,21-23]. However, it is highlighted that there is an increasing interest in their potential unexplored use and therefore an urgent need for qualitative and quantitative deepening into this sector [3,7]. In particular, there are few studies that examine the use of herbs and herbal medicine for the prevention and treatment of upper and low GI diseases and most importantly the vast majority of them are characterized by inadequate methodology, small sample sizes, short term duration, poor quality results and lack of confirming data [21-24]. What is more, they are very heterogeneous and frequently subjected to publication bias [9], not to mention that most of the results derive from either in vitro protocols or preclinical animal testing. Thus, it is crucial that herbs and their future use as preventive medical tools or therapeutic medicine be the subject of larger, well designed clinical studies with high quality and validity (randomized double-blinded placebo-controlled) to obtain more conclusive results that could be incorporated in standard medical care [19,21,25]. To this end, herbal therapeutic substances and remedies should undergo a rigorous testing as potential pharmaceutical drugs, being very cautious when extrapolating and interpreting the data from in vitro studies to in vivo protocols [26], as the possible interaction of the specific constituents and the safety aspects of such herbal remedies may be very heterogeneous, inconclusive and alternating [9,14,27].

In particular, there are many herbs and extracts that have been examined for their effect in the GI system, bust most data can be found in the IBS and IBD symptoms' management [7,21-23,28]. Most studies on herbs and extracts include single preparations such as Aloe vera, Curcuma species, peppermint oil (which is commonly used, as both a component of prescription medicine and as a constituent of several over-the-counter remedies and is supposed to be beneficial) [21,29], turmeric extract, artichoke leaf [23], cannabinoids [30], mastic gum, tormentil extracts, wormwood herb [25], *boswellia serrata* [31], as well as compound preparations which seem to be more effective compared to single ones such as Carmint, Chinese herbal medicine, Padma Lax, STW 5 (also known with the trade name Iberogast) [23,24,29], Tong-xie-ning,Tong-Xie-Yao-Fang,C-IBS and DA-IBS formulations [21,22,28]. It is worthy to highlight that the US National Center for complementary and Integrative Health has gathered in a series of brief fact sheets basic information about more than 50 specific herbs or botanicals [2]. while World Health Organization has developed and launched a new project called "WHO Traditional Medicine strategy 2014-2023" in order to promote policies and implement action programs that will strengthen the role of traditional medicine in improving population's health [3]. Furthermore, even fewer data can be collected for the upper GI disorders, as it is reported that active chemical constituents (e.g. tannins and flavonoids), contained in various medicinal plants and their extracts, could have significant antiulcer activity [32], an assumption which derives from *in vivo* experiments on animal models or traditional folk medicinal use to treat gastric infections, mainly by targeting *H. pylori* [33,34]. Moreover, it is also supposed that the combination of extracts rather than single components appears to be more effective and promising [7,21,24], especially when it comes to heterogeneous or not fully understood pathological conditions such as functional dyspepsia [23,25].

Socio economic Perspective

Apart from the afore mentioned, there are many more arguments in favour of investing more research opportunities in this field [3,12,14]. To begin with, herbs and herbal treatments are common practices of traditional medicine for various GI diseases in the developing world where there is a lack of sufficient equipment, supplies and human resources [4-6]. Therefore, it is of paramount importance that those traditional applied therapies be scientific examined and founded in order to be used in a wider scale and substantially contribute to the improvement of life quality in underdeveloped countries, where common gastrointestinal disorders can lead to mortality [6]. From socioeconomic perspective, it is also vital to highlight the financial burden that most times is related with such diseases as their management or treatment is generally long term, expensive [36] and unaffordable for many people [37,38]. On the other hand, the cost of herbal therapy will be probably smaller than that of conventional treatment, and this constitutes a key reason for international scientific societies and government organizations [3,12] to financial support the conduction of clinical studies that promote locally available opportunities of drug development with herbs [13]. It would not be very optimistic to declare that pharmaceutical companies must aid to the current knowledge by supporting relevant studies even if their financial gain would be much lower compared to other kinds of treatment, as they are already moving to this direction (roughly 50% of new chemical entities introduced during the past two decades are from natural products) [12,14,26].

Nutritional Perspective

Except for the socioeconomic conditions that indeed prove the need for more research on that field, special attention should be given on the fact that herbs may have added value, mainly because of their natural origin, their nutritional characteristics and interaction with basic human's regulatory and functional mechanisms [21,22,26]. To be more specific, as to the Digestive and Gastroenterology system, it is often claimed that individual chemical substances derived from plants may have antibacterial [34], antioxidant, anti-inflammatory [39], and immunoregulatory properties [21]. Most theories support that those characteristics can have significant value in this specific system through various mechanisms that are related to the regulation of neurotransmitters and hormones in the enteric nervous system, modulation of smooth muscle motility in the gastrointestinal tract [8], modulation of the hypothalamic-pituitary-adrenal axis, attenuation of intestinal inflammation and restoration of intestinal flora, inhibition of specific modulators, antiplatelet activity [8,25] etc.

Things to consider

There are additional things to consider and examine, when it comes to the manufacture of herbal medicine and their integration in standard medical care either as supplementary of first line treatment [8,9,18,19]. To begin with, quality control is very important [30],

as the practices that accompany the conversion of a herb to a medicine as well as the critical hazards are many and should always be very careful defined and implemented [27]. To this end, there are many examples that highlight the need for clear and evidence based frameworks and legislations [3,14,24], such as the environmental conditions that can affect the composition and the concentration of the active ingredients of plant extracts, the specification of the ideal handling and storage practices or the combination of the chemical families with possible medicinal utility [30,40]. What is more, the exact concentration and dose of the constituents of commercial herbal products is another aspect which needs detailed and rigorous investigation, as well as the analytical description of possible interactions of herbal and conventional medicines [26]. Under this umbrella, authenticity and homogeneity of herbs and strict regimes of physical processing and extract manufacturing are critical factors to maintain phytochemical consistency in commercial products [3,14]. It goes without saying that in order to ensure both safety and efficacy of herbal medicine, implementation of and adherence to good agricultural and collection practice, good plant authentication and identification practice, good manufacturing practice before and during the manufacturing process, and good laboratory practice in analysis are necessary [8,41].

Apart from this, there are numerous plants and herbal extracts that may have a therapeutic impact, yet being unknown, unexplored, limited studied or a part of oral traditional knowledge in local livelihoods and tribes still not widespread [4,5]. In the last occasion, the potential exploitation of herbal remedies by developed world for medical reasons requires a compliance to sustainability goals [6] and environmental preservation in order for flora not to be endangered by intense exploitation [1]. As to the unexplored species and components which may have beneficial health outcome, new facts are always emerging and are under examination [14] with promising results such as Bromelain, that has been shown to have anti-inflammatory activities *in vitro* [31] or specific WEFs which could have many uses because of their phytochemical, toxicological and pharmaceutical potential [4].

Last but not least, herbals – like all drugs – may have side effects which must be further explored, especially when they are prescribed to people with other comorbidities [2,3,9,12,13]. Until recently, most of the published trials showed no serious side effects, as the number and type of the adverse events were similar or fewer than placebo or conventional treatment [2,3,42]. Those effects are limited to minor events like nausea or diarrhea, although it is likely that some of the herbals could lead to serious renal and liver morbidity (eg, hepatic failure) [43], not to mention that is urgent to dive into the long-term safety of herbal treatment, as possible mutagenicity, toxicity and carcinogenicity has not adequately be explored and thus cannot be excluded [4,31,43]. However, it should be pinpointed that in specific GI disorders such as IBD, most of the published herbal therapies appear to have minimal adverse effects so far [3,42].

Conclusion

In conclusion, there is a need for research based and clinically tested knowledge as to the potential pharmaceutical uses of plants, herbs and their extracts in order to acquire deeper understanding of their impact to human's health and to ensure that their future integration in conventional medical practice will only be implemented after safety, sustainability and health topics are satisfied. This applies not only to the IG diseases but to all body systems that pharmaceutical plants could have added value. It is crucial to realize that there are many opportunities and promising points in this unexplored area, which until recently lacked in scientific background, research foundation and institutional support.

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