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The relationship between the cold and dry nature of herbs and their tannin content: Bridging traditional knowledge and modern-day science

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ABSTRACT: According to Persian Medicine (PM), the primary qualities of herbs or their nature play a crucial role in their medical applications. Objective: This library-based study aimed to determine the association between plants' tannin content and their cold and dry nature considered by ancient Persian philosophers. Methods: plants with cold and dry nature were extracted from monographs of Makhzan al-Adviyah and Tuhfat ul-Momineen, the latest and the most comprehensive ancient Persian pharmacopeias. For determining the mentioned pants tannin content, scientific search engines were explored. Results: the results of this study were shown in a Table 1 containing 53 herbs with cold and dry temperament, providing their Persian and scientific names and medicinal parts, belonging to thirty-six botanical families. Table 1 also presented the tannin content of herbs (hydrolysable and condensed tannins). Five out of fifty-three herbs were not backed with any scientific evidence to contain tannins. Among the botanical families, Solanaceae, Fabaceae, Rosaceae, and Poaceae were repeated several times in which tannins could be assumed as their chemotaxonomic markers. Thus, temperaments could predict chemotaxonomic markers of herbs. Furthermore, there was an overlap between medical applications of herbs with their cold and dry nature and their pharmacological activities, including anti-hemorrhoid, anti-helminthic, anti-diarrhea, buccal ulceration, and gastro-protective. Tannin-containing plants with cold and dry nature could be explored to indicate unidentified pharmacological activities. Conclusion: Philosophical approaches of PM could be the fundamentals of medical discoveries to fill the gap between traditional and conventional medicine regrading chemotaxonomy markers, phytochemical studies, and pharmacological activities of herbs.

KEYWORDS: Conventional medicine; nature; Persian traditional medicine; tannin; temperament; traditional medicine.

1. INTRODUCTION

Herbs and herbal preparations are the principal sources of medicine, and their utilization is tied with the history of humankind and ancient civilizations. Herbal medicine is the foundation of traditional medical schools. In crude terms, diverse traditional medicine systems provide approaches to herbs and natural products. In recent years, combining traditional and conventional medicine has worked to improve clinical experiences. It has been beneficial in drug screening, discovery, and development [1]. Moreover, World Health Organization (WHO) has devised various plans and strategies to strengthen the role of traditional medicine in improving public health and wellness. However, approval of some parts of traditional medicine based on philosophy requires critical examination. Thus, integrating traditional and conventional medicine approaches necessitates in-depth research [2].

Persian Medicine (PM) is one of the most ancient schools studied and practiced by ancient Persian physicians. Similar to other traditional systems, it has some fundamental and underlying concepts which are not recognized and applied in modern medicine. Conceptualization of PM considers temperament (*midzaj*) for each food and medicament, whether plant-derived or mineral substance [3]. The theory of temperaments is the basis of major traditional medicine systems, including Unani (Greek), Arabic, Roman, Indian, European, Chinese, and Persian. The roots of this theory go back to ancient Greece, where Hippocrates (460–370 BC) and Galen (129-200 AD), two outstanding physicians of history of medicine, developed it. According to this concept, four elements (fire, soil, water, and air) make up the whole world. The ratio between these elements

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determines that objects temperament (*midzaj*). Different temperaments of plants cause them to exhibit various pharmacological effects in therapy. These effects are interpretable concerning the aforementioned fundamental elements in their composition [4]. Searching for convergence between traditional and contemporary medicine could lead to employing encrypted information from ancient literature to enrich modern science. As stated in PM pharmacopeias, each medicament obtained from herbal, animal, or mineral sources has a specific primary quality or nature, which determines its function in the body.

Prior studies have noted the contribution of phyto-constituents and herbs' typical nature raised in PM [5]. However, far too little attention has been paid to tannin- containing medicinal plants with cold and dry nature. The objectives of this paper are first to compile the herbs with cold and dry temperaments and elucidate whether or not they contain tannins. Second, to find any association between the natures of herbs, their botanical families, and their tannin content as their chemotaxonomic marker. Third, to find any correlation between ancient medical applications of cold and dry plants and their modern-day pharmacological effects.

This study could provide the potential for new studies and pave the way for further research on herbs. Thus, new biologically active compounds and unknown pharmacological effects could be found.

2. RESULTS

Table 1 provides 53 herbs with Persian and scientific names, belonging to 36 botanical families, their medicinal parts used for medical applications, their tannin content, and tannin type (condensed or hydrolyzable tannins).

Table 1. The list of herbs containing cold and dry nature according to Persian manuscripts.

No.	Persian name	Scientific name	Family	Medicinal part	Tannin content[1]	Tannin type	R
1	Aconitun	*Aconitum napellus*	Ranunculaceae	Root	+	NM[2]	[9]
2	Afes/mazoo	*Querqus infectoria*	Fagaceae	Galls	+	H[3]-C[4]	[10]
3	Afyoon	*Papaver somniferum*	Papaveraceae	Latex	NM	NM	NM
4	Aghti	*Sambucusnigra/ S. ebulus*	Caprifoliaceae	Berries	+	H-C	[11, 12]
5	Ahlilaj	*Terminalia chebula Retz.*	Combretaceae	Fruit	+	H-C	[13, 14]
6	Ambarbaris	*Berberis vulgaris*	Berberidaceae	Fruit	+	H-C	[15]
7	Amole	*Phyllanthus emblica*	Combretaceae	Fruit	+	H-C	[16, 17]
8	Anjebar	*Polygonum bistorta*	Polygonaceae	Rhizome	+	H-C	[18]
9	As	*Myrtus communis L.*	Myrtaceae	Leaves, fruits, seeds	+	H-C	[19]
10	Asalghaz	*Tamarix Spp.*	Tamaricaceae	Leaves	+	H	[20]
11	Ash-anghur	*Rhamnus spp.*	Rhamnaceae	Root	+	NM	[21]
12	Balilaj	*Terminalia bellirica*	Combretaceae	Fruit	+	H	[22]
13	Banafsaj	*Viola odorata L.*	Violaceae	Flowers, leaves	+	-	[23, 24]
14	Banj	*Hyoscyamusniger L.*	Solanaceae	Leaf	NM	NM	NM
15	Bish	*Aconitum heterophyllum*	Ranunculaceae	Root	NM	NM	NM
16	Bonn	*Coffea arabica L.*	Rubiaceae	Bean	+	H-C	[25]
17	Chenaar	*Platanusorientalis L.*	Platanaceae	Leaf & bark	+	C	[26]
18	Choobchini	*Smilax china L.*	Liliaceae	Rhizomes	+	NM	[27]

19	Daleek	*Rosa canina L.*	Rosaceae	Fruit	+	C-H	[28]
20	Daarvan	*Azadrichta indica*	Meliaceae	Leaf, bark, seed, and flower	+	H-C	[29, 30]
21	Faufal	*Areca catechu L.*	Arecaceae	fruits	+	C-H	[31]
22	Ghabira (Senjed)	*Elaeagnus angustifolia*	Ebenaceae	Seeds, fruits, leaves	+	C	[32-34]
23	Hamahem	*Ocimum basilicum*	Labiatae	All parts	+	H-C	[35, 36]
24	Hinna	*Lawsonia inermis L.*	Lythraceae	Leaf	+	H-C	[37]
25	Holab	*Bupleurum exaltatum*	Apiaceae	All parts	NM	NM	NM
26	Inab al- thalab	*Solanum nigrum*	Solanaceae	Whole plant	+	NM	[38]
27	Jar-ol-nahr	*Beta vulgaris*	Chenopodiaceae	Leaves and roots	+	C-H	[39-41]
28	Javras (Arzan)	*Panicum miliaceum*	Poaceae	Seed	+	C	[42]
29	Joz al masal	*Datura stramonium*	Solanaceae	All parts	+	NM	[43]
30	kafur	*Cinnamomumcamphora*	Lauraceae	bark	NM	NM	NM
31	kakonaj	*Whitaniasomnifera*	Solanaceae	Root	+	H	[44, 45]
32	Kharnub	*Ceratoniasiliqua L.*	Fabaceae	Pod	+	C-H	[46]
33	Khelaf	*Salix alba*	Salaxaceae	Bark	+	C-H	[47]
34	Khollar	*Lathyrussativus L.*	Fabaceae	Seed	+	C	[48]
35	Kuzbara	*Coriandrumsativum L.*	Apiaceae	Seed, leaves	+	C	[49,50]
36	Moghilan	*Acacia arabica*	Fabaceae	All parts	+	H-C	[51]
37	Ojen	*Syzygiumcumini*	Myrtaceae	Fruit	+	C-H	[52]
38	Otroj	*Citrus medica L.*	Rutaceae	fruits	+	NM	[53]
39	Oyarsalam	*Cyperusesculentus L.*	Cyperaceae	root	+	-	[54]
40	Roman	*Punicagranatum*	Punicaceae	Root, peel, flowers	+	C-H	[55]
41	Seel (margh)	*Cynodondactylon (L.)*	Poaceae	All parts	+	C	[56]
42	Samrat-ol-tarfa (Ghaz)	*Tamarix spp.*	Tamaricaceae	Flower, leaves, roots, galls	+	H	[57]
43	Sandal	*Santalum album L.*	Santalaceae	heartwood	+	C	[58]
44	Sedr/Konar	*Ziziphusspina-christi*	Rhamnaceae	Leaves	+	C	[59]
45	Shokaran	*Conium maculatum L.*	Apiaceae	All parts	+	NM	[60]
46	Somagh	*Rhuscoriaria*	Anacardiaceae.	Fruits	+	C-H	[61]
47	Tabashir	*Saccharumsponteneum*	Poaceae	Whole plant	+	NM	[62]
48	Taj khorous	*Amaranthus Spp.*	Amaranthaceae	Leaf, Seed	+	NM	[63]
49	Tamr-e- hendi	*Tamarindusindica L.*	Fabaceae	Fruit	+	C	[64]
50	Torshak	*Rumex spp.*	Polygonaceae	Aerial parts	+	C-H	[65]

51	Ward-ahmar	*Rosa damascena*	Rosaceae	Flowers	+	C-H	[66-67]
52	Zaroor	*Crataegousazarolus L.*	Rosaceae	Fruits	+	C-H	[68]
53	Zereshk	*Berberis vulgaris*	Berberidaceae	Fruit	+	C-H	[69]

[1] the plants with tannin contents were shown with a ((+)) sign, and those not containing tannins were shown as NM.
[2] Not Mentioned
[3] Hydrolysable tannins
[4] Condensed tannins

3. DISCUSSION

The presented Table can be revealing in several ways. According to Table 1, 53 species belonging to 36 botanical families were compiled via exploring PM pharmacopeias. As it is apparent, tabulated plants belong to various families. However, among the mentioned plants, there are four plants belonging to Solanaceae, four to Fabaceae, four to Rosaceae, and three to Poaceae. These results can be associated with biochemical systematics. Biochemical systematics, molecular taxonomy, or chemotaxonomy is an expanding discipline providing chemical evidence to interrelate plants. Among phytochemical markers, polyphenolic compounds are of profound value. Hydrolysable tannins take center stage as taxonomic markers of the Rosaceae family. As mentioned in previous studies, oligomeric hydrolysable tannins, comprising monomers of hydrolysable tannins, are highly likely to be phytochemical markers of Rosaceae family. In Solanaceae, Fabaceae, Poaceae, or related species, various hydrolysable and condensed tannin groups could be introduced as significant chemotaxonomic phyto-constituents. Therefore, temperament of herbs according to PM manuscripts have the potential to predict phytochemicals which are important in case of taxonomy. Further studies are needed to verify particular types of tannins as markers in other botanical families and genus, which can pave the way for more studies related to biochemical systematics [70].

This manuscript offers the relationship between herbs' cold and dry temperament and their tannin content. Traditional medicines' theories and concepts, typically the ones related to Persian Medicine (PM), are based on herbs' primary qualities and their temperaments. According to these fundamental qualities, plants are categorized as hot, cold, wet, and dry. Simple temperaments are compounded to result in twosome temperaments of herbs, namely, hot and dry, cold and dry, hot and wet, cold and wet. The predominance of qualities in each subject determines the temperament or *midzaj* of that herb. Since ancient philosophers or physicians did not have access to instruments, they explained the functional mechanism of herbs according to their temperament. Phytochemical studies of herbs can assist in deciphering the temperaments of herbs. These studies could also determine new paths to unraveling phytochemistry and the pharmacological effects of herbs [4].

In PM, the medical functions of herbs are named *afaal*. *Afaal* or medical functions of herbs originated from twosome temperaments of medicinal plants. Thus, herbs with cold and dry temperaments indicate typical medical functions. Ancient physicians assigned them astringent (*ghabez*) and restraint material that can cure thrush aphtha. They can prevent several dentistry problems such as loosening teeth and gums and bleeding in buccal cavity. They are also mentioned to treat hyperhidrosis, to be anti-diarrhea, anti-rhinorrhagia, anti-hemorrhage, anti-pyretic, anti-vertigo, anti-dementia, anti-cephalgia, anthelmintic, stomachic, and appetizer agents. Tannin-containing medicinal herbs were prescribed to cure intestinal ulcers and epiphora.

According to the findings of modern medicine, tannins are astringent (*ghabez*) polyphenols that take center stage in the defensive mechanisms of plants against pests or other microorganisms. They also possess numerous medical and pharmacological applications. Tannins are bactericides, anti-bacterial, anti-viral, and anti-fungal agents. Similarly, they have been used a long time to treat bacterial infections such as urinary infections. Since indicating immuno-modulatory, anti-inflammatory, and antihistaminic effects, also regulating secretion of the cytotoxins, tannin-containing herbs were used to control asthma and rhinitis. Hence, they possess an antidiarrheal effect due to induction of reabsorption of electrolytes and increasing transit duration in the gut. Moreover, tannin-containing herbs and tannin derivatives could inhibit inflammatory mediators which assist in anti-diarrheal properties. Also, tannins have shown anti-spasmodic and gastro-protective effects. In other words, tannin-containing herbal extracts are utilized to calm gastritis and gastric ulcers [71]. They indicated anthelmintic, antioxidant, anti-hypertension, anti-diabetic, and cardio-protective effects. They were used to soothe hemorrhoid problems with anti-oxidant and wound healing

effects. As astringent agents, they are applied to prevent buccal ulceration and bleeding of the gums. Furthermore, previous studies illustrated the anti-proliferative and cytotoxic effects of tannin derivatives [72].

The comparison of medical applications of tannins in modern medicine and their applications in PM reveals overlaps between these applications. There is a correlation between some applications of tannin-containing plants in both schools of modern and traditional medicine (**Figure 1**). These findings have important implications for developing investigations in the pharmacological pipeline. In crude terms, tannin-containing plants with cold and dry nature could be explored to indicate unidentified biological and pharmacological activities.

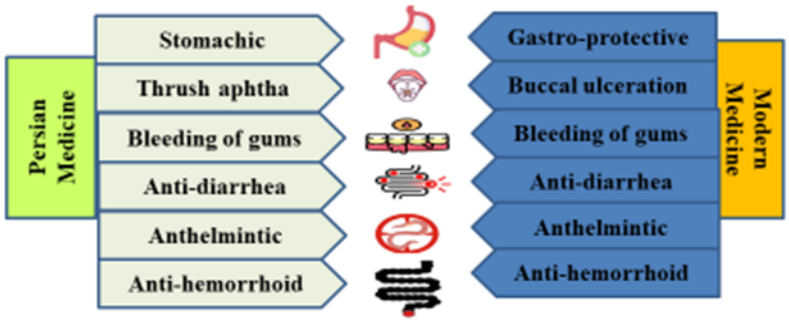

Figure 1. The correlation between medical applications of cold and dry herbs and tannin-containing medicinal plants.

As shown in Table 1, another important finding was that five out of fifty-three plants with cold and dry temperaments were not backed with any evidence regarding tannin content. These plants include *Papaver somniferum*, *Aconitum heterophyllum*, *Hyoscyamu sniger*, *Cinnamomum camphora*, and *Bupleurum exaltatum*. There are two possible explanations for this result; first, tannin-related phytochemical screening has not been carried out on these herbs. Second, the mentioned test was carried out; however, they did not indicate any tannin content. It goes without saying that, as it is apparent in **Table 1**, some plants were shown to contain tannins using preliminary phytochemical screening tests; however, the tannin type was not clear. These results could open up a new avenue of research regarding identifying and isolating diverse types of tannins which might be introduced as phytochemical markers in those herbs.

4. CONCLUSION

This study set out to translate concepts and knowledge of PM into modern medicine. Even though ancient philosophers did not have access to the developed instruments to identify phytoconstituents, their theories based on quadratic elements and definition of temperaments assisted them to cure patients. Thus, philosophical approaches of PM could be the fundamentals of evidence base or modern medicine discoveries. Also, these studies could fill the gap between traditional and conventional medicine and open up new avenues of research on phytochemistry, chemotaxonomic markers, pharmacological activities, drug discoveries, and development from botanical sources.

5. MATERIALS AND METHODS

The latest and most comprehensive PM pharmacopeias were used in this library-based study. First, Makhzan al-Adwiyah (Mohammad Hussein Aghili Khorasani, 18th century A.D.) was investigated, one of the comprehensive manuscripts comprising 1721 monographs (mineral, herbal, and animal-based) with their temperaments. The monographs include the medicines commonly addressed by PM physicians. Among the medicines, herbs with cold and dry temperaments were selected 5. Second, Tuhfat ul-Momineen (Momen Tonekaboni, 17th century A.D.), one of the notable manuscripts of PM, was explored for medicinal plants with cold and dry nature. The mentioned pharmacopeias are the latest and complete PM Pharmacopeias where single drug monographs with herbal, animal, and mineral origins are described. Each monograph comprises a description, habitat, temperament, indications, drug dosage, and its substitutes [6, 7]. Besides, for elucidation of the tannin content of compiled herbs, the current literature search was carried out using scientific search engines, namely PubMed, Web of Science, Scopus, and Google scholar. The summary of this study led to a table comprising herbs' Persian and scientific names, family, their medicinal parts, tannin content, and the type of tannin.

Tannin compounds, secondary plant metabolites, are a class of biologically-active and astringent ingredients that play a vital role in protecting plants against predators. These large polyphenolic compounds assist in plant growth regulation. Regarding the chemical structure of tannins, they fall into two major categories: hydrolyzable and condensed tannins (proanthocyanidins or catechins tannins). Regarding hydrolyzable tannins, they encompass a polyalcohol core in which hydroxyl groups are esterified with gallic acid named gallotannins or terahydroxydiphenic acid called ellagitannins. The structure of these compounds could be various owing to intermolecular oxidative linkages. Weak acids and high temperatures give rise to the hydrolyses of these phytoconstituents. In contrast to condensed tannins, the occurrence of hydrolyzable tannins are limited to Angiospermae and dicotyledons [8]. The second group, proanthocyanidins or condensed tannins, occurs highly in the plant kingdom. These polyphenols are result of C4-C8, C6–C8, and C-O-C linkage between monomers of catechins (flavan-3-ol and flavan-3, 4-diol). These oligomeric and polymeric phytochemicals are not hydrolyzed. Therefore, these compounds' decomposition yields phlobaphens, which are reddish phenolic compounds. (**Figure 2**)

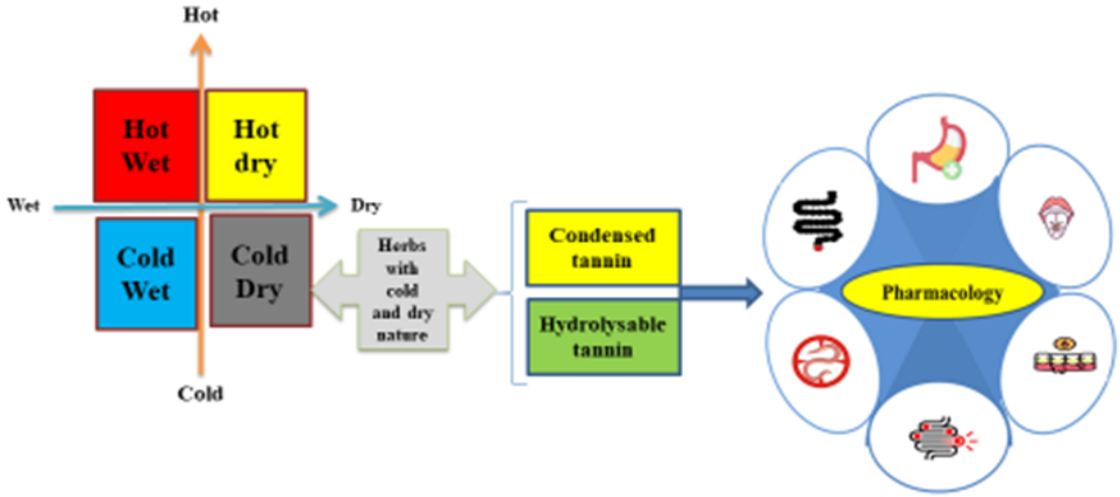

Figure 2. Graphical abstract

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