

Medicinal Herbs Useful in Pediatric Fever from the Perspective of Persian Medicine

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Abstract

Background

Fever is the most important and common symptom of pediatric diseases. Fever can be a sign or symptom or complication of disease. Considering the development of complementary and alternative medicine worldwide and the prevalence of this symptom in children, we aimed to investigate their application based on Persian medical textbooks by searching herbs used in pediatric fever.

Materials and Methods

In this review study, materials were extracted by searching in reliable Persian medical textbooks of the 10th -20th century using related Persian medicine keywords. Then the documentations for herbs extracted were searched in the databases based on the conventional medicine. The interpretation was made based on the results.

Results

Based on the Persian medical textbooks, seventeen herbs have been prescribed for decreasing pediatric fever. Among them, 16 herbs have proven mechanisms of action for treatment of fever, classified into five categories (diaphoretic, anti-inflammatory, anti-septic, immunomodulatory, anti-oxidant) based on literature review. On the other hand, according to Persian medicine, there were thirteen cold temperament herbs and only four hot temperament ones. They were administrated using various oral and topical methods. The maternal and neonatal treatment was emphasized.

Conclusion

According to this study and documentations of conventional medicine, many of these herbs can be effective in the treatment of pediatric fever, so further clinical studies are recommended for evaluating their efficacy.

Key Words: Fever, Herbal Medicine, Pediatric, Persian Medicine, Medicinal plants.

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1- INTRODUCTION

Fever is one of the most common clinical symptoms in children, which accounts for 30% of their visits to the physician (1-3). The normal body temperature is between 36 and 37.5°C, varying between 0.5 and 1.0 degrees during the day. There is no accurate definition of fever due to these normal changes; fever occurs at temperatures above 38 °C (100 °F). However, it should be noted that the type of body temperature measurement is also important. The armpit, ears, and foreheads are simpler, but they are less accurate and may need to be confirmed by oral and anal methods (4, 5).

Based on conventional medicine, fever is considered as a sign and symptom for diseases, and is caused by a change in the hypothalamus temperature. Fever is a complication of diseases and its cause may sometimes remain unknown during diagnostic procedures (6, 7). To treat fever, physician must first eliminate the underlying cause of the fever directly, rather than eliminating fever itself. Fever is associated with almost all infectious diseases, but also occurs in diseases such as neoplastic, autoimmune, metabolic or endocrine, granulomatous disorders, inflammatory bowel disease (IBD), drug reactions, infarction or vascular thrombosis, as well as trauma. Many studies have supported the role of fever in increasing the types of host defense, yet physicians commonly prescribe antipyretic treatments (8).

On the other hand, there is sometimes fever of unknown origin (FUO), which refers to prolonged fever and no cause can be found for it during diagnostic evaluations (9). Based on Persian medicine (PM, Iranian traditional medicine), fever itself is considered as a disease and it is an abnormal heat that is ignited in the heart or in another member, from which it comes to the heart and then spreads throughout the body through blood circulation and warms

it to the extent that normal actions are disrupted. Fever is a disease that can occur independently, or may be a complication of another disease or turn into a different disease (10-13). In all PM textbooks, a large chapter is devoted to the fever that discusses a variety of fevers. In pediatric fever, in spite of the child's treatment, in cases where the infant is breastfed, mother's underlying condition should also be treated in order to modify the mother's milk (10).

Considering that the principles of treatment in PM are based on lifestyle modification and the use of medicinal herbs in local and oral forms in one hand, and today attempts are being made in many societies to further expand complementary medicine in order to provide healthcare services, on the other hand; it is essential to become familiar with medicinal herbs that have been prescribed by prominent Persian traditional scholars such as Avicenna and Rhazes for the treatment of pediatric fever from thousands of years ago, and recent studies have proved the antipyretic effects of some of these herbs. Therefore, in this article, in addition to the introduction of effective medicinal herbs in pediatric fever from PM textbooks, the mechanism of their action in recent studies will be discussed.

2- MATERIALS AND METHODS

In this study, effective herbs in pediatric fever were extracted from the reliable PM textbooks of 10-20th century such as *al-Hawi*, *Qanon in Medicine*, *Zakhireyeh Kharazmshahi*, *Makhzan Aladvieh*, *Exir-e-Azam* (it was written in recent years), now taught in PM schools (**Table.1**), using the related Persian and Arabic keywords including *homma*, *hommayat*, *tab*, *bacheh*, *afal*, *teb-e sonnati*, *daruhaye giahi*. Then, databases such as Medline (via PubMed), Scopus and Google Scholar were searched using the keywords of fever, pyrexia, hyperpyrexia, herbal medicine, and

traditional medicine, child, children, and pediatric. Time period of our research was from 2000 up to now. Attempts were then made to investigate the mechanisms of these herbs on reducing fever, extract their similarities and differences, and categorize them. It is noticeable that inclusion criteria

were the herbs which in PM are used for fever control in children. Moreover, they should be mentioned in at least one textbook. For exclusion criteria, the herbs without specific scientific name, the herbs with unknown identity, and unmentioned herbs in our textbooks were excluded.

Table-1: Persian Medicine manuscripts used in this study.

No.	Persian/Arabic names of the manuscripts	English/Latin names of the manuscripts	Author	Date written	Subject of manuscripts
1	<i>Al-Hawi</i>	Liber Continent	Rhazes	10 th Century CE	Medical Encyclopedia
2	<i>Al-Qanun fi al-Teb</i>	The Canon of Medicine	Avicenna	11 th Century CE	Medical Encyclopedia
3	<i>Zakhireyeh Kharazmshahi</i>	Treasure of Kharazmshah	Jorjani	12 th Century CE	Medical Encyclopedia
4	<i>Makhzan Aladvieyh</i>	Storehouse of Medicaments	Aghili	17 th Century CE	Herbal Encyclopedia
5	<i>Exir-e-Azam</i>	Great Elixir	Nazim Jahan	20 th Century CE	Medical Encyclopedia

3- RESULTS

When PM textbooks were searched, a total of 17 antipyretic herbs were found that were arranged in alphabetical order according to their scientific name (**Table.2**). In addition to the scientific and Persian names of herbs, it includes the family name, the mechanism of the antipyretic action of the herbs, the temperament of the herbs, and its mode of application. Herbs were classified into several groups based on the mechanism of antipyretic action (**Table.3**). Of the 17 antipyretic herbs, there was no new evidence suggesting *Citrullus lanatus* (Thunb.), Matsum and Nakai effectiveness in reducing fever. For the rest of the plants, all of the antipyretic mechanisms are presented based on recent studies (**Tables 2, 3**). Results of recent studies and PM textbooks are presented below.

3-1. The antipyretic mechanism of herbs in recent studies

Based on recent studies for the above herbs, 5 mechanisms are effective in

reducing fever including antiseptic, anti-inflammatory and analgesic, diaphoretic and antipyretic, immunomodulatory and antioxidant mechanisms. Some herbs such as *Portulaca oleracea* L. and *Glycyrrhiza glabra* L. have been effective in reducing fever through all mechanisms, but some other herbs have two or more mechanisms (14-18). The most common fever-reducing mechanism was antiseptic (including antibacterial, antiviral, antifungal and antiparasite) that included 14 herbs. The second common mechanism was an anti-inflammatory and analgesic mechanism with 13 herbs. The third one was diaphoretic and antipyretic mechanism seen in 10 herbs. There were 7 herbs having antioxidant effects and 6 cases with immunomodulatory effects (14, 15, 19).

3-2. The antipyretic mechanism of herbs in Persian medicine

PM, a comprehensive school, is based on temperaments and humors with history of more than a thousand years. It considers different temperaments and humors *Dam*

(Blood), *Safra* (Yellow bile), *Balgham* (Phlegm), *Soda* (Black bile) for the human body. The presence of each of these humors reflects the corresponding quality. The qualities of the above humors are respectively as follows: hot & wet, hot & dry, cold & wet, and cold & dry. In a healthy state, there is a balance between these humors, and the imbalance in these humors leads to an imbalanced temperament and a dystemperament (Suezizaj), which ultimately leads to the disease (11, 20). Since Persian traditional scholars defined a certain temperament for all herbal, animal, and mineral drugs, they also prescribed a medicine to treat dystemperament. Although there are various fevers in PM, elevated body

temperature is common in all of them. According to this view, people who have hot temperament are more susceptible to fever (10). With regard to the herb's temperament, 13 out of 17 herbs have cold temperament and 4 herbs (*Matricaria chamomilla* L., *Mentha piperita* L., *Glycyrrhiza glabra* L., *Beta vulgaris* L.), also have hot temperament. According to PM, these herbs are consumed as follows: oral as decoction (6 herbs), syrup (2 herbs), distilled (1 herb), vegetable and juice (1 case for each one), inedible as footbath (5 herbs), rectal suppository (2 herbs), topical use with oil (2 herbs), and poultice (1 herb). Four herbs were usable in two ways (**Table.2**).

Table-2: The list of herbs mentioned in the Persian Medicine textbooks for pediatric fever.

Scientific name (21)	Common name (22)	Persian name (22, 23)	Family (21)	Modern medicine	Temperament of herb (11, 23)	Mode of application based on Persian medicine (10, 11)
<i>Althaea officinalis</i> L.	Marshmallow	<i>Khatmi</i> /khætmi/	Malvaceae	Antipyretic (even topical) (3), Anti-inflammatory, Antibacterial, Antifungal (24, 25).	Cold	Footbath, Rectal suppository
<i>Beta vulgaris</i> L.	Beet	<i>Choghondar</i> /tʃoghondær/	Amaranthaceae	Antioxidant, Anti-inflammatory (26, 27), Due to: Betanin (26, 27), Immunomodulatory, (28).	Hot	Footbath
<i>Cichorium intybus</i> L.	Chicory	<i>Kasni</i> /ka:snɪ/	Compositae	Anti-inflammatory, Antibacterial, Antiallergic, Antihepatotoxicity (29).	Cold	Oral (Decoction, distilled by product)
<i>Citrullus lanatus</i> (Thunb.) Matsum. & Nakai	Water melon	<i>Hendevaneh</i> /hendevɑ:nɜ:/	Cucurbitaceae	Not found.	Cold	Footbath
<i>Coriandrum sativum</i> L.	Coriander	<i>Geshniz</i> /geʃni:z/	Apiaceae	Antibacterial (30, 31), Antifungal (30), Anti-inflammatory (31, 32), Analgesic (32), Antioxidant (31), Due to: Linalool, decrease in NO production, increase in noradrenaline and serotonin (32).	Cold	Oral (Decoction)
<i>Fumaria officinalis</i> L.	Fumitory	<i>Shahtareh</i> /ʃɑ:htærɜ:/	Papaveraceae	Antibacterial (33), Antioxidative, Hepatoprotective (34).	Cold	Oral (Decoction)
<i>Glycyrrhiza glabra</i> L.	Licorice	<i>Shirin bayan</i> /ʃi:ri:n bæja:n/	Leguminosae	Analgesic (35), Antipyretic (36), Anti-inflammatory (16, 35-39), Antibacterial (16, 38), Antiviral (16, 37-39), Antifungal (37), Antioxidant, Immunomodulatory (16, 36, 38, 39), Anti-helicobacter pylori (36), Hepatoprotective and cardioprotective effects (16).	Hot	Oral (Decoction)
<i>Lawsonia inermis</i> L.	Henna	<i>Hana</i> /hæna:/	Lythraceae	Antibacterial, Antifungal (40-43), Antiviral, Antiparasite (42, 43), Healing skin wounds and infections (40), Antioxidant (42, 44), Anti-inflammatory, Analgesic (43).	Cold	Topical (Poultice)

<i>Matricaria chamomilla</i> L.	Common chamomile	<i>Babouneh</i> /ba:bu:nɜ:/	Compositae	Anti-inflammatory, Antibacterial, Diaphoretic and antipyretic, Immunomodulatory (14, 15, 19, 45), Due to: Inhibits production of cyclooxygenase and lipooxygenase and so prostaglandins and leukotrienes (19).	Hot	Topical (Oil)
<i>Mentha piperita</i> L.	Peppermint	<i>Nanaa</i> /næna:	Lamiaceae	Species of this family like: <i>M. piperita</i> L./ <i>M. pulegium</i> L/ <i>M. longifolia</i> (L.) L.: Prevention of infectious diseases and anti-infective, Antipyretic (14, 15), Anti-inflammatory, Antibacterial, Antifungal, Antiparasite (19, 46-48), Analgesic (49), Spasmolytic (50).	Hot	Oral (Decoction), Topical (Oil)
<i>Nymphaea alba</i> L.	Waterlily	<i>Niloufar</i> /ni:lu:fær/	Nymphaeaceae	Species of this family like: <i>N. alba</i> L./ <i>N. lutea</i> (L.) Sm./ <i>N. Stellata</i> : Antipyretic, Analgesic, Immunomodulatory (51), Antiseptic, Antibacterial (52), Anti-leishmanial (52, 53).	Cold	Oral (Syrup)
<i>Plantago major</i> L.	Great plantain	<i>Barhang</i> /ba:rɦæŋg/	Plantaginaceae	Anti-inflammatory, Anti-infective, Antipyretic (54), Antibacterial (55).	Cold	Oral (Syrup)
<i>Portulaca oleracea</i> L.	Common purslane	<i>Khorfeh</i> /kɦorfɜ:/	Portulacaceae	Immunomodulatory (56), Antioxidant, Antipyretic (57, 58), Anti-inflammatory (17, 56-58), Analgesic (17, 58, 59), Antiseptic (58).	Cold	Oral (as vegetable)
<i>Punica granatum</i> L.	Pomegranate	<i>Anar</i> /æna:r/	Lythraceae	Anti-inflammatory, Due to: COX-2 inhibitory and reduce PG-E2 by Polyphenols And Tannins (43), Antibacterial (60-65), Antifungal (61, 66), Antiviral (65), even for antibiotic resistance (60).	Cold	Oral (Juice)
<i>Salix species</i>	White willow	<i>Beed</i> /bi:d/	Salicaceae	Antipyretic, Antibacterial, Healing Skin wounds (67), Due to: containing salicylates, but not oral for children (68).	Cold	Footbath
<i>Viola odorata</i> L.	Sweet violet	<i>Banafsheh</i> /bæna:fʃɜ:/	Violaceae	Anti-inflammatory, Antibacterial (gram negative), Antioxidant, Antipyretic and for FC of children (69, 70), Antiviral (71), Antifungal (70), Due to: Salicylic acid, Cyclotide protein (70-72).	Cold	Footbath, Rectal suppository
<i>Ziziphus jujube</i> Mill.	Jujube	<i>Onnab</i> /ɔna:b/	Rhamnaceae	Anti-inflammatory, Antipyretic, Expectorant, Enhancement of Natural Killer Cells' activity, Antiallergic (73-75), Due to: Inhibition of cyclooxygenase-2 and prostaglandins (76), Anti- <i>Helicobacter pylori</i> (43).	Cold	Oral (Decoction)

Table-3: The mechanisms of action of herbs mentioned in the Persian Medicine textbooks for pediatric fever.

Mechanism	Diaphoretic, Antipyretic	Anti-inflammatory, Analgesic	Anti-septic (bacterial / viral / fungal / parasite)	Immunomodulatory	Anti-oxidant
<i>Althaea officinalis</i> L.	+	+	+		
<i>Beta vulgaris</i> L.		+		+	+
<i>Cichorium intybus</i> L.		+	+		
<i>Citrullus lanatus</i> (Thunb.) Matsum. & Nakai					
<i>Coriandrum sativum</i> L.		+	+		+
<i>Fumaria officinalis</i> L.			+		+
<i>Glycyrrhiza glabra</i> L.	+	+	+	+	+
<i>Lawsonia inermis</i> L.			+		+
<i>Matricaria chamomilla</i> L.	+	+	+	+	
<i>Mentha piperita</i> L.	+	+	+		
<i>Nymphaea alba</i> L.	+	+	+	+	
<i>Plantago major</i> L.	+	+	+		
<i>Portulaca oleracea</i> L.	+	+	+	+	+
<i>Punica granatum</i> L.		+	+		
<i>Salix species</i>	+		+		
<i>Viola odorata</i> L.	+	+	+		+
<i>Ziziphus jujube</i> Mill.	+	+		+	

4- DISCUSSION

This article is the first review study that investigates effective herbs for reducing fever in children based on PM textbooks. This article examines the current evidence suggesting the effectiveness of these herbs in treating fever. In this research, 17 herbs were extracted from PM textbooks, both therapeutic and herbal Pharmacopoeia (10, 11, 23). These medications were administered orally and topically to the infants or children and, as diet for mothers who breastfed their infants. Based on this theory, in the infant's fever, food orders are also prescribed to the breastfeeding mother

because the Persian traditional scholars believe that if the mother is ill, her milk will not be of good quality and can cause disease for her infant, and even a ban was applied on breastfeeding in the case of severe maternal diseases (10). Although there was no similar finding on prescribing medications to a mother to treat her infant's fever in any of the current related articles, the prohibition of breastfeeding in Human T-lymphotropic Virus Type 1 (HTLV-1) positive mothers is approved in recent studies (77). According to PM textbooks, lifestyle and nutritional modification are very important in the treatment of diseases, and if the disease is

not eliminated, medicinal plants are prescribed in the next step (10-12). The remarkable thing to note in this study was that, despite the various kinds of drug in PM, such as animal or mineral origin, or opiate drugs such as poppy syrup in treating fever, herbal remedies were used to treat the pediatric fever more frequently than other medications of animal, mineral or opiate origin (10); which indicates that the Persian traditional scholars were aware of the use of drugs with less complications in children.

The most common antipyretic mechanism in extracted articles is antimicrobial agents (including bacteria, viruses, parasites, and fungi), and according to PM, it can be interpreted that efforts have always been made to cure the primary cause of the disease and not symptomatic treatment. So, the fever can be eliminated by removing the microbial agent. The second mechanism is the anti-inflammatory and analgesic mechanism, and herbs that act based on this mechanism are effective in inhibiting inflammation by controlling the cyclooxygenase 2 enzyme and production of prostaglandin E2. The third mechanism decreases the body temperature in the febrile patient through sweating and subsequent evaporation and some herbs contribute to the process by increasing sweating. The fourth and fifth mechanisms are immunomodulatory and antioxidant functions. They act via improvement of immune system, which can be effective not only in infectious diseases, but also in other febrile diseases (11, 19).

Considering the fact that the majority of the herbs had cold temperament (13 cases), it can be stated that in order to cope with fever due to hot dys temperament, many cold temperament herbs can be effective. Other justification may be cold temperament of herbs that can reduce inflammation by anti-inflammatory pathways as explained previously. On the other hand, there were 4 hot temperament

herbs, which, according to PM can eliminate fever by removing its causative agents. Although this finding requires further clinical and complementary studies (10, 11). There are clinical studies only on *Althaea officinalis* L. and *Viola odorata* L. out of antipyretic herbs whose mechanism of action is discovered. Ebadinezhad et al. (3) in 2016 have proved that the footbath with decoction made from *A. officinalis* L. is effective in reducing fever. Feyzabadi et al. (69) in 2017 referred to the effect of *V. odorata* L. on febrile convulsion in children. Mohsenzadeh et al. (14) in 2016 in a similar review article searched for the herbs used in pediatric fever, however, the results are collected based on the recent studies and no search was made in Persian medical books.

Saeidnia et al. (15) in 2009 referred to the pediatric fever, and here the methodology is based on recent studies. Contrary to previous studies, antipyretic herbs were searched in the present study based on the reliable PM textbooks, and then the recent documentations were extracted and the mechanism of potential effects of these plants on reducing fever was presented. Although, of the 17 herbs, there was no evidence suggesting the *C. lanatus* efficacy in reducing fever in recent studies, according to PM, watermelon has a cold temperament, and watermelon-based footbath may have been used to help cool the body (23).

Considering the effectiveness of some of these herbs in reducing the pediatric fever, further clinical studies are needed to prove the antipyretic effects of remaining herbs. One of the strengths of this study is that there has been no similar study on antipyretic herbs for children based on PM textbooks. Recent articles only recommend a treatment for the febrile babies but not for the breastfeeding mother or breastfeeding ban, while treatment of breastfeeding mother is also recommended in PM. The weaknesses of this study are

that no relationship was found between herbal temperaments and the antipyretic mechanisms in the conventional medicine considering the low number of herbs used. Proving the effectiveness of these plants requires clinical trials on children.

5- CONCLUSION

The present research is the first narrative study for investigating the effectiveness of herbs in pediatric fever control by PM textbooks. The result of this study showed that the mentioned herbs have not been used in clinical approaches. For example, although pomegranate (*Punica granatum*) is a fruit that can relieve the fever, there is not a processed drug based on it for treatment of fever. Relevant to the effectiveness of most of these herbs in reducing fever in recent studies, further clinical studies are recommended for the production of natural products based on these herbs to be prescribed along with common treatments for pediatric fever. Considering the aboriginal status of these herbs in Iran, their cheap prices, lower complications, and the public willingness to use complementary medicine, further research is required.

6- CONFLICT OF INTEREST: None.

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