

Herbal Appetizer for Children with Failure to Thrive (FTT) in View of Traditional Persian Medicine: A Review

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Abstract

Background

Failure to thrive (FTT) is a condition of poor weight gain in early childhood. Low appetite which is associated with FTT interacts with increasing caloric intake as the main treatment for FTT. Phytochemicals in herbal remedies could alter appetite more than the expected effects of other nutrients. This review aimed to assess the effective and safe herbal appetizer for children with FTT according to Traditional Persian Medicine (TPM).

Materials and Methods

By searching through major pharmaceutical books of Persian medicine during 8th -18th centuries (A.D.), herbal remedies as appetizer were determined. We searched the phytochemical and pharmacological activities of these herbs in PubMed, Scopus, Web of Sciences and Google scholar databases, from 1950 to 15 December 2016.

Results

Overall, 42 herbs were found. Among these herbs, only 11 herbs were prescription for children. Improvement of feed intake, growth performance, weight gain and gastro-esophageal protection were the most reported activities.

Conclusion

Natural remedies prepared from these herbs may be useful for enhancing appetite especially for FTT in children. Additional well-designed studies are required to investigate the safety and efficacy of these herbs.

Key Words: Appetite, Children, Herbal Medicine, Failure to Thrive, Persian Medicine, Traditional.

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1- INTRODUCTION

Failure to thrive (FTT) is a condition of poor weight gain and growth of any age, especially in infancy and early childhood (1). FTT exists in all socioeconomic groups with the relative priority incidence in lower income communities (2). As a result of negative effects of FTT on children in terms of a long-term sequel of developmental delay, micronutrient deficiencies, and suboptimal linear growth, it is noticeably important to treat these deficiencies (3-6). Majority of cases secondary to inadequate nutrition whether medical, or psychosocial problems lead to FTT (7). According to parent's reports, 20% of children showed eating disorders during childhood (8). Although increasing caloric intake is the main treatment for FTT, low appetite associated with FTT interacts with this treatment (9, 10). Majority of studies demonstrate the effectiveness of the intervention in terms of applied behavior analysis in treatment of feeding disorders (11, 12).

Cyproheptadine has been used for improving feeding behaviors and weight gain. This drug has its own side effects (13). It is believed that herbal medicines are relatively safer and have fewer side effects than other medicines (14). In recent years, there has been an increasing tendency through using herbal supplements in diseases all over the world (15). The use of herbal medicines is also common in children (16, 17). Phytochemicals that are found in herbal remedies could alter appetite beyond the expected effects of other nutrients (18). Many herbs have been introduced in Traditional Persian Medicine (TPM) for enhancing appetite and maybe useful for children with FTT. Mechanisms of action for some of these plants are known. This study was conducted to extract the traditional herbal appetizers from Persian

medicine literatures on the basis of new researches.

2- MATERIALS AND METHODS

The main books of TPM and herbs advised for increasing appetite were selected according to the following criteria:

- Author's reputation,
- Historical coverage (a thousand year ranging from about 800 to 1800 A.D),
- Repetition of herbal administration (at least in two textbooks).

According to these criteria, the following books were selected: *Al-Hawi fi al-tibb* (The Liber Continents) by Rhazes (865-925 A.D.), *Al-Qanun fi'l-Tibb* (The Canon of Medicine) by Avicenna (980-1037 A.D.), *al-Abnih 'an Haqaeq al Adwia* by Abu Mansur Movafaq ibn Ali al-Heravi (10th century)', *Tuhfeh-ye Hakim Mu'min* by Mir Muhammad Mu'min Husaini Tonekaboni (1669 AD), known as *Hakim Mu'min* and *Makhzan-Al-Advie* by Aghili Khorasani (1772 AD). *Shahvat* (which means appetite) and *Moshahhee* (which means appetizer) were the specific main key words used for searching herbs in traditional textbooks (19-23).

The next step was designed for evaluating the safety of these herbs in children according to new herbal books and electronic databases. The other search was performed using electronic databases including PubMed, Scopus, from 1900 to 15 December 2016 to find any *in vitro*, animal or clinical evidence for the efficacy of each of these herbs and the relevant pharmacological activities supporting their effectiveness in appetite enhancing. The search keywords used included scientific or common name of each plant with "appetite", "ghrelin", "neuropeptide Y", "growth", "weight", "leptin", "serotonin", "gut hormones", "nesfatin-1", "Vaspin",

"apelin", "visfatin", and "cholecystokinin". Language restriction was performed, and only studies in Persian or English languages were considered in this study.

3- RESULTS

3-1. Appetite mechanism in conventional medicine

Appetite regulation includes two components: homeostatic which shows daily energy requirement for sustaining bodily functions and hedonic which means pleasures and desires for food (24). The arcuate nucleus (ARC) in the

hypothalamus regulates food intake and energy expenditure with two populations of neurons that show an opposite effect (stimulant or inhibitor) to one another. The medial parts contain orexigenic neurons that act as orexigenic neurons that express neuropeptide Y (NPY), and agouti-related protein (AgRP). The lateral side of ARC act as anorexigenic neurons that express alpha-melanocyte-stimulating hormone (α -MSH) derived from Pro-opiomelanocortin (POMC), and cocaine and amphetamine-regulated transcript (CART) (Figure.1) (25, 26).

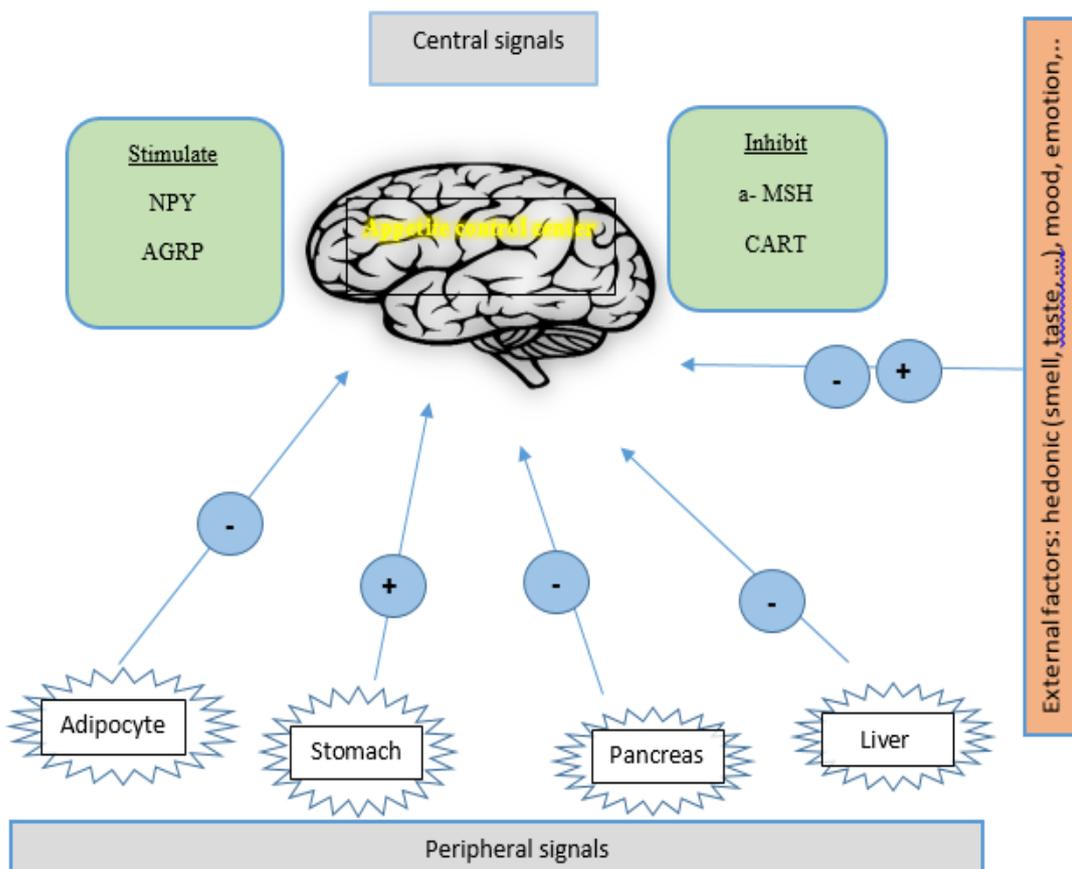


Fig.1: Changes in appetite and food intake by stimulant or inhibitor signals.

Moreover, neuronal circuits, circulating gastrointestinal and adipocyte hormones are involved in this regulation (27). Information signals from peripheral organs are sent to the hypothalamus by vagal afferent pathway and circulation (28). Ghrelin is a stimulating appetite hormone, predominantly found in the stomach (29, 30). Ghrelin also carries out other functions such as regulation of growth hormone (GH), gastric acid secretion, and gut motility (31-33). Increase in food intake has been shown in obese and lean subjects after intravenous administration of ghrelin (34), while other gut peptides such as peptide YY, cholecystokinin, oxyntomodulin (OXM), and glucagon-like peptide-1 (GLP-1) have a reducing role on appetite pathway (35-37). Visceral adipose tissue has an endocrine function, with the secretion of many adipokines such as leptin, and adiponectin (38).

Leptin has an ability to reduce appetite and body weight in lean as well as obese rats (39). Leptin serum levels increased in a BMI-dependent manner in patients with anorexia nervosa (AN) after refeeding (40). Vaspin, a new adipokine, have shown higher levels in serum of girls with restrictive anorexia nervosa compared to the control group (41). Other adipokines such as visfatin and apelin had lower levels in underweight children compared to normal group and should be considered in the etiology of anorexia (42).

3-2. Appetite mechanism in TPM

According to Traditional Persian Medicine, existence is formed by four groups of elements, which are symbolically named fire, air, water, and earth. Every element has its specific quality for example, fire is hot and dry, air is hot and moist, water is cold and moist, and soil is cold and dry. The combination of these elements with different ratios makes the temperament. So every being has its own quality which is dependent on

the most dominant element existing in its structure (43, 44). The temperament has an important role in maintaining the ideal healthy state of an individual. Dystemperament in humans result from imbalances in healthy temperament, and may lead to organ dysfunction and disease. Humor is a biochemical composition originating from disposition of foodstuffs in stomach towards liver and blood vessels (45). Four natural humors in the body are related by pairs of qualities: Sanguine is hot and wet, bile is hot and dry, phlegm is cold and wet and melancholy is cold and dry (46). In TPM, having an appropriate appetite is considered as a sign of health. The main organs which are involved in this regulation are stomach, liver and brain. Every dystemperament in whole body or in these organs may lead to loss of appetite. In most cases, hot dystemperament in the heart or excess cold dystemperament in whole stomach is the main responsibility in the loss of appetite. Cold weather can enhance the appetite in contrast to hot weather. Melancholy is increased in the stomach when an individual is in a state of hunger. Fundus is sensitive to melancholy, so this humor can stimulate the appetite. This sensation may be lost because of brain disorders or neural involvement. Melancholy is considered as a sour taste. Sleep and mood affect the appetite (22, 47).

3-3. Herbal appetizers in TPM

The most common plants which have been recommended by TPM to enhance appetite are shown in **Table.1**. Forty two herbs were known as appetite enhancing herbs with majority of were from *Lamiaceae* followed by *Rosaceae* and *Apiaceae*. Only sumac and citron were mentioned as appetite enhancers in all 5 main TPM texts. Other herbs such as peach, apple, quince, olive, lettuce, radish, mastic, onion were followed as more cited herbs in these texts and most of these plants were not considered as healthy in children. There is

no available data on the safety of many herbs in children. However, a search on pediatrics herbal books, herbal monographs, resources and databases showed that 11 herbs including apple, quince, olive, peppermint, mint, chickpea, lettuce, radish, coriander, flixweed and onion were identified as safe for children (**Table.1**). Although wormwood is advised for enhancing appetite in children through phytotherapy in paediatric books and widely used in many countries; the European Medicines Agency (EMA) does not recommend the use for children due to lack of sufficient data (59). There are few studies on the therapeutic effects of these herbs on appetite enhancing. We could not find randomized clinical trials about orexigenic pathway for them. Hence, other positive effects on gastrointestinal organs and weight gain were considered. These findings are presented in **Table.2** (*please see the tables 1 and 2 in the end of paper*).

3-3-1. *Allium cepa* L.

Onion, a species of the genus *Allium*, is probably native of south west Asia (76). According to TPM, onion is a herbal appetizer which has tonic effect on digestive system (19). Onion possesses noticeable health beneficial substances such as the flavonoid (mainly quercetin). Quercetin may protect against cardiovascular disease, and cancer (77). Organosulfur compounds have been associated with anthelmintic, antiseptic and hypoglycemic effects of onion (76). These compounds have been linked to lowering of cholesterol levels and blood pressure (78). High levels of antioxidant compounds (polyphenolics) in onion have protective effects against different degenerative agents (79).

Onion has been used in animal feed as digestion stimulants and growth promoters. An et al. investigated the effects of onion extract on growth performance of broilers. Chicks were

divided into four groups and experimental diets (non-medicated diets containing 0.3 or 0.5% onion extract), or fed control diets (non-medicated commercial diet or medicated antibiotics) for 5 weeks. Weight gain of the group fed by non-medicated control diet was lower than those fed by medicated control group. Weight gain of broiler chicks fed with 0.3 or 0.5% onion extract was as similar as medicated control group (68).

3-3-2. *Coriandrum sativum* L.

Coriander has been widely used for the treatment of different disorders such as loss of appetite, insomnia, vertigo, airways and digestive disorders. In TPM, it is considered as a tonic for stomach, heart and brain (19, 23). Coriander is prescribed for enhancing appetite in children in recent books (50). Various cases have reported the allergenicity of coriander (80, 81). Sensitivity to the Apiaceae family (coriander, caraway, fennel, celery) of spices was reported to be high following skin prick tests in children (< 15 years old), and adults (82). According to European Food Safety Authority (EFSA), "coriander seed oil" as a novel food ingredient (NFI) is not aimed towards children (83). The main bioactive compounds present in coriander are lipids (containing fatty acids, sterols, and tocopherols), polyphenols and essential oils (84). Many studies have shown the medicinal effects of coriander as a sedative-hypnotic, antioxidant, anxiolytic, analgesic, and anticonvulsant, gut modulatory, and diuretic herb (85-88).

Nematy et al. investigated the effect of *Coriandrum sativum* (coriander) hydroalcoholic extract on rat appetite. They divided thirty male wistar rats randomly into five groups. One of the two control groups received 0.5 ml of water per day (vehicle group), the other one did not receive anything (control group). The other 3 groups were treated daily with 50, 100 or

150 mg/kg of coriander for 7 days. There was a significant change in energy intake after treatment by 100 and 150 mg/kg of the extract in comparison to other groups. This study indicated that coriander had positive effects on appetite of rats (69).

3-3-3. *Artemisia absinthium* L.

Wormwood is considered as a tonic for stomach, liver and whole body and used as an *anti-helminthic* in TPM. It is administrated for enhancing appetite and stomach ache (22, 23). Several trials demonstrated the advantageous effects of wormwood for the treatment of many diseases condition such as lead exposure, inflammatory periodontal disease, Crohn's disease (89-91). Wormwood has phytochemicals such as phenolic and flavonoids compounds. These compounds may contribute to its anti-oxidative activity (92). Thujone, a bicyclic ketone terpene, is a major active ingredient of wormwood which was blamed for his side effects such as seizures. Risk assessment of Thujone in foods and medicines showed that there is no risk associated with the occasional medicinal use of wormwood or sage (93, 94). Although wormwood is indicated for appetite in Pediatric Phytotherapy hand book, the European Medicines Agency (EMA) did not recommend the use for children under 18 years of age (50, 59). Taraghdari et al. investigated orexigenic effect of *Artemisia absinthium* in rats. Rats were randomly divided into five groups. Control group did not receive anything and Vehicle group received 0.5 ml of water per day. All 3 remaining groups received 50, 100 and 150 ml of wormwood. The results showed that in comparison to the control group, there were no significant ($p > 0.05$) differences in energy intake (receive) before and during intervention between three case groups. In this study, data showed ineffective and dose-related result of wormwood on appetite of rats (70).

3-3-4. *Mentha spicata* L.

Mint is a well-known herb in TPM. Tonic effect of spearmint on stomach and reducing stomach bloating has been mentioned in TPM in terms of useful consequences on nausea, vomiting, hiccup and belch. Spearmint, especially with pomegranate, considerably enhances appetite (22, 23). The aromatic herbs of the "mint" group include taxa of the Lamiaceae family. All of them have rich essential oils in *p-menthane* compounds (95). Mint is mostly taken after a meal due to its ability to reduce indigestion and intestinal spasms by reducing the gastrocholic reflux (96). *M. spicata* possesses several biological activities such as antimicrobial and antioxidant activities as well as being quite rich in phenolic components (97, 98). In an animal study, impact of different levels of spearmint was investigated on performance in broiler diets. Birds were fed with four levels of spearmint of 0, 1, 1.5, and 2%. Average feed intakes obtained from the experiment were 2680.20, 2679.11, and 2708.55, respectively. Nevertheless, the body weight gains for the treatments were 1481.63, 1512.81, 1519.57, and 1519.63, 0, 1, 1.5 and 2, respectively. As a result of feed intake, there is body weight gain of broiler which is enhanced by the supplementation of different levels of spearmint to the diets (71). Khurshid et al. investigated the effect of peppermint on performance in broiler diets in five groups. Group (T1) is considered as control, without additives in diets whereas T2 and T3 were fed with raw mint leaves 1% (T2), and 2% (T3). In T4 and T5, enzyme treated mint leaves, 1 and 2% were added to the basal diet. In comparison to control group, birds that received diet supplemented with either raw and enzyme treated mint leaves gained significantly ($p < 0.05$) higher live body weight. There was a significant ($p < 0.05$) improvement in cumulative feed conversion ratio in all the treatment groups when compared with the control (99).

3-3-5. *Olea europaea*

The Olive tree is a native of the Mediterranean basin and parts of Asia and now it is widely cultivated in many other parts of the world (10). According to TPM, olive is considered as a tonic for stomach and enhancing appetite when used during meals (23). The presence of high content of monounsaturated fatty acid (MUFAs), and functional bioactives including carotenoids, phospholipids, tocopherols, and phenolics, with multiple biological activities in olive oil are the main reasons ascribed to the health benefits of olive oil (101, 102). Olive fruit contains hydrophilic (phenolic acids, phenolic alcohols, flavonoids and secoiridoids), and lipophilic (cresols) phenolic compounds that are known to possess multiple biological activities such as anticarcinogenic, antioxidant, antimicrobial, anti-inflammatory, anti-dyslipidemia, anti-hypertensive, cardiogenic, laxative, and antiplatelet. Pectin, organic acids, and pigments are other important compounds present in olive fruit (103).

Olive leaf extract shows gastro-protective activities against experimentally induced gastric lesions by absolute ethanol in mice. Administration of 40, 80, and 120 mg/kg olive leaf had similar protective effect to reference drug ranitidine given to the positive control at a dose of 50 mg/kg, intragastrically (104). Odabasoglu et al. evaluated the effects of vegetable oils (corn, olive and sunflower oils), and alpha-tocopherol on anti-inflammatory, and gastrointestinal profiles of indomethacin in rats. Indomethacin given with sunflower, corn, and olive oils reduced paw edema induced by carrageenan by 79.5, 74.0, and 60.5%, whereas individual indomethacin and diclofenac reduced paw edema by 56.2, and 50.7%, respectively. These oils and alpha-tocopherol effectively improved the levels of antioxidant defense systems in rat stomach tissues against oxidative

damage (72). Gastroprotective activity of *Hypericum perforatum* L. maceration in three: oils sunflower (E1), olive (E2), and palm oil (E3), was evaluated by using cold-restraint stress (CRS) induced rat gastric mucosa lesions test. Contrary to the lowest quercetin content, HPE prepared with olive oil (E2) showed the highest protection against gastric damaging action of CRS (73).

3-3-6. *Cydonia oblonga* Mill

Quince as a fruit has been used in TPM to increase appetite. According to TPM, it has tonic effects on stomach, brain and heart, and may be useful in liver weakness (23). The quince is a native of Iran, and Turkey, but it is now found in other places (104). Quince has significant health promoting values and activities, including phenolic composition, antioxidant capacity, anti-inflammatory, anti-allergic, anti-microbial, anti-carcinogenic, anti-ulcerative, and it might also act as a tonic for brain and heart (106). It is an appropriate source of vitamin C and minerals especially calcium, magnesium, potassium, and phosphorus. Moreover, quince contains organic acids, sugars, and fatty acids. Quince is considered as a suitable source of polyphenols due to the high intensity of astringency and bitterness of this fruit even at ripening stage (106).

Aqueous ethanol extracts of quince fruit have been shown to exhibit anti-*Helicobacter pylori* activity (108, 109). Tansaz et al. evaluated the anti-gastroesophageal reflux effect of *Cydonia oblonga* Mill fruit extract in a pilot study. After one month administration of quince extract to 5 infants with reflux and without any response to routine management, four of them had significant changes in the symptoms of reflux including vomiting, cough, agitation and low appetite. They concluded that because of the astringent property of quince, it can reinforce the sphincter and inhibit the reflux (74).

Zohalinezhad et al. evaluated the efficacy of quince syrup in pediatrics with symptomatic gastro-esophageal reflux disease. In this study, symptoms were reduced in quince compared to control group (receiving omeprazole), but no significant differences were found between two groups (65).

3-3-7. *Malus domestica* Borkh.

Apple is a well-known fruit in TPM with many beneficial effects on main organs such as heart, brain, liver, and stomach. Apple with astringent effect on the heart helps the stomach and enhances appetite (18). Polyphenols which are found in apple have a wide range of biological activities with a role in prevention of chronic diseases (75). Flavonoids, a major class of phytochemicals found commonly in apple, have an inverse relationship with coronary mortality in women (110).

Current data suggest that apple might be linked to reduced risk of many diseases such as lung cancer, asthma and cardiovascular disease. Apple may also influence outcomes related to diabetes, bone health, Alzheimer's disease, cognitive decline of normal aging, weight management, and gastrointestinal protection from drug injury (111). Carrasco-Pozo et al. evaluated the protective effect of apple peel polyphenol extract (APPE) against gastrointestinal damage in rats treated with indomethacin. An increase in malondialdehyde concentrations and decrease in the ratio of reduced glutathione (GSH) to oxidized glutathione (GSSG) following administration of APPE protected the gastric, intestinal, and colonic mucosa from oxidative stress. APPE also showed anti-inflammatory effects as evidenced by the lower myeloperoxidase activity (75).

4- DISCUSSION

Medical help is often favorable for children with poor appetite and growth.

However, there are few studies that have evaluated the effects of herbal extracts on appetite (112). The current study conducted a scientific evaluation to find the relevant pharmacological activities supporting the effectiveness of TPM-recommended plants on appetite enhancing. In TPM, having appropriate feeding behaviors are considered as nutritional orders for everyone. Central Nervous System (CNS) has a main role in appetite and any disturbance.

Hence, behavioral therapy and emotional control are the first step in the treatment of appetite disease according to TPM scholars. Recent researches mentioned the role of many G protein coupled receptors (GPCRs) in the oral cavity and gastrointestinal tract acting as taste receptors. The gastrointestinal tract can sense basic tastes in the same manner with the tongue in most cases. In health, these receptors control the secretion of gut hormones and the expression of nutrient transporters to maintain energy and glucose homeostasis and gastrointestinal function through sense nutrients from a luminal and then transmit them as well; any disturbances or adaptations in the expression or sensitivity of these taste receptors and their signaling pathways in disease may affect digestive behavior and metabolism. Evidences suggest that bitter agonists could be considered as suitable targets to reduce hunger and motility (113). The identity of the sour taste sensor is still unknown (114).

According to TPM, sour taste helps to create a good appetite. Studies for evaluating relationship between sour taste receptors and ghrelin or other signaling hormones, in future are advisable. This study had a clear limitation which was not considering all of the related literature in other foreign languages and unpublished data. Despite the widespread use of medicinal herbs, their administration is doubtful because of insufficient studies

about safety and drug interactions especially in children. Further studies are required to make a decision about the helpfulness and safety of these herbs.

5- CONCLUSIONS

Appetite enhancing natural medicines with repeated traditional reports may be appropriate sources of new drug discovery. These natural medicines may introduce new ways in the treatment of children and adolescence diseases with low appetite such as anorexia in cancers. Additional pharmacological and clinical studies will open new ways for better understanding of the exact mechanisms through which these plants and their ingredients act.

6- CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

7- ACKNOWLEDGMENTS

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Table-1: Medicinal Plants Indicated for enhancing appetite in TPN

Family	Scientific name	Common name	TPM name	Family	Part used	References	Administration for children
Amaryllidaceae	<i>Allium cepa</i> L.	Onion	Basal	Hot and dry	Bulb	Can/Mak/Tuh/Abn	Could be administrated (47)
Amaryllidaceae	<i>Allium ampeloprasum ssp persicum</i>	Leek	Korras	Hot and dry	Seed	Mak/ Tuh	No evidence found
Anacardiaceae	<i>Mangifera indica</i>	Mango	Anbaj	Hot and dry	Fruit as a pickle	Mak/ Tuh	No evidence found
Anacardiaceae	<i>Pistacia lenticus</i> Desf.	Mastic tree	Mastakee	Hot and dry	Oleogum Resin	Can/Mak/Tuh/ Haw	No evidence found
Anacardiaceae	<i>Rhus coriaria</i> L.	Sumac	Somagh	Cold and dry	Fruit	Can/Mak/Tuh/Abn/ Haw	No evidence found
Apiaceae	<i>Carum carvi</i> L	Caraway Celery	Ceravia	Hot and dry	Fruit	Mak/ Tuh	Not recommended
Apiaceae	<i>Apium graveolens</i> L.	Celery	Karafs	Hot and dry	Herb, seed	Mak/ Tuh	No evidence found (48)
Apiaceae	<i>Coriandrum sativum</i> L.	Coriander	Kozbore	Hot/ Cold and dry	Leaf	Mak/ Tuh	Could be administered (49)
Apiaceae	<i>Trachyspermum ammi</i>	Ajwain,	Nankhah	Hot and dry	Fruit	Mak/ Tuh	Safety is not known (50)
Asteraceae	<i>Artemisia dracunculus</i> L.	Tarragon	Tarkhoon	Hot and dry	Leaf	Mak/ Tuh	Insufficient available evidence (51)
Asteraceae	<i>Tanacetum parthenium</i> (L.) Sch. Bip.	feverfew	Oghhovan	Hot and dry	Flower	Mak/ Tuh/ Abn	Not recommended in children younger than 2 years (52)
Asparagaceae	<i>Hyacinthus Tourn.ex</i> L.	Hyacinth	Sonbol	Hot and dry	Flower	Mak/ Tuh	No evidence found
Berberidaceae	<i>Berberis vulgaris</i>	Barberry	Anbarbaris	Cold and dry	Fruit	Mak/ Tuh/ Abn	Not recommended (53)
Brassicaceae	<i>Alyssum homolocarpum</i>	Alyssum	Ghoddoumeh	Hot and wet	Seed	Mak/ Tuh	No evidence found
Brassicaceae	<i>Descurainia sophia</i> (L.) Webb ex Prantl	Flixweed	Khobbe	Hot and wet	Seed	Mak/ Tuh	Could be administered (54)

Brassicaceae	<i>Raphanus satives</i>	Radish	Fojl	Hot and dry	Seed/leave	Can/Mak/Abn/ Haw	Could be administered (49)
Cannabaceae	<i>Cannabis sativa</i>	Hemp	Ghennab	Cold and dry	leave	Mak/ Tuh	Not recommended (55)
Combretaceae	<i>Terminalia bellirica</i> (Gaertn.) Roxb	Bastard myrobalan	Balilaj	Cold and dry	Fruit	Mak/ Tuh	Not recommended (56)
Compositae	<i>Lactuca sativa</i> L.	Lettuce	Khas	Cold and wet	Leaf	Can/Mak/Tuh/ Haw	Could be administered (57)
Compositae	<i>Artemisia absinthium</i> L.	Wormwood	Afsantin	Hot and dry	Herb (seed, flower, leaf)	Can/Mak/Tuh/ Haw	Controversy (49, 58)
Fabaceae	<i>Cicer arietinum</i> L.	Chickpea	Hemmas	Hot and dry	Seed	Mak/Tuh	Could be administered
Lamiaceae	<i>Mentha pulegium</i>	Pennyroyal	Foodanaj	Hot and dry	Flower/ leaf	Can/ Haw	Not recommended(59)
Lamiaceae	<i>Mentha spicata</i> L.	Mint	Naana barree	Hot and dry	Leaf	Mak/Tuh	Could be administered (59)
Lamiaceae	<i>Satureja hortensis</i> L.	Summer savory	Marzeh	Hot and dry	Herb, seed	Mak/Tuh	Insufficient available evidencence (60)
Lamiaceae	<i>Zataria multiflora</i> Boiss	Saatar	Saatar	Hot and dry	Herb, seed) flower)	Mak/Tuh	No evidence found
Lamiaceae	<i>Ziziphora clinopodioides</i> Lam.	Wild Thyme	Moshktrameshee/ Kakouty	Hot and dry	Herb	Mak/Tuh	No evidence found
Moraceae	<i>Morus nigra</i>	Black mulberry	Shahtut	Cold and dry	Fruit	Can/Mak/Tuh/ Haw	Not enough scientific evidence to safely (61)
Oleaceae	<i>Olea europeae</i>	Olive	Zeytoon	Hot and dry	Fruit	Can/Mak/Tuh/ Haw	Recommended
Polygonaceae	<i>Rheum ribes</i> L.	Rhubarb	Reebass	Cold and dry	Root	Mak/Tuh	Not recommended (62)
Polygonaceae	<i>Rumex conglomeratus</i> Murray	Clustered dock	Torshak	Cold and dry	Fruit	Mak/Tuh/ Haw	No evidence found
Phyllanthaceae	<i>Phyllanthus emblica</i>	Emblie or myrobalan	Amelaj	Cold and dry	Fruit	Can/Tuh/ Haw	No evidence found
Rosaceae	<i>Crataegus microphylla</i> K.Koch.	Hawthorn	Zaroor	Cold and dry	Fruit	Mak/Tuh	Not recommended (63)
Rosaceae	<i>Cydonia oblonga</i> Mill.	Quince	Safarjal	Cold and dry	Fruit	Can/Mak/Tuh/ Haw	Could be administered (64)

Rosaceae	<i>Malus domestica Borkh.</i>	Apple	Toffah	Sweet: hot and wet	Fruit	Can/Mak/Abn/ Haw	Adminestrated
Rosaceae	<i>Prunus cerasus</i>	Sour Cherry	Ghaarasia	Cold and dry	Resin	Mak/Tuh/ Haw	No evidence found
Rosaceae	<i>Prunus persica</i>	Peach	Khookh	Cold and wet	Fruit	Can/Mak/Tuh/ Haw	May cause allergy (65)
Rutaceae	<i>Citrus aurantium L.</i>	Bitter Orange Peel	Narenj	Hot and dry	Sweat of flower	Mak/Tuh	Not recommended (66)
Rutaceae	<i>Citrus medica L.</i>	Citron	Otroj	Hot and dry /cold and dry	Rind of fruit/fruit	Can/Mak/Tuh/Abn/ Haw	No evidence found
Rutaceae	<i>Ruta graveolens L.</i>	Common Rue	Sodaab	Hot and dry	Leaf	Can/Mak/Tuh	No evidence found
Vitaceae	<i>Vitis vinifera L.</i>	Vine grape Verjuice	Hesroum	Cold and dry	Vinegar Sauce	Mak/Tuh	No evidence found
Zingiberaceae	<i>Curcuma zedoaria (Christm.) Roscoe</i>	Zedoary	Jadvar	Hot and dry	Rhizome	Mak/Tuh	No evidence found

Can: Canon, Haw: Al-Hawi fi al-tibb, Abn: al-Abniah, Tuh: Tuhfeh-ye Hakim Mu'min, Mak: Makhzan-Al-Advie.

Table-2: Studies on medicinal plants used for enhancing appetite in Traditional Persian Medicine

Plant name	Pharmacological activities	Fractions and phytochemicals	References
<i>Allium cepa</i>	Improving broiler weight gain and growth performance in broiler chicks fed with 0.3% or 0.5% onion extract as similar as medicated control group. Weight gains of the group fed non-medicated control diet were lower than those of medicated control group.	0.3% or 0.5% onion extract for 5 weeks.	(67)
<i>Coriandrum sativum</i> L.	A significant change in energy intake and appetite after treatment by 100 and 150 mg/kg of the coriander extract in comparison to control groups on rat.	Hydroalcoholic extract.	(68)
<i>Artemisia absinthium</i> L.	There was no significant ($p>0.05$) differences in energy intake before and during intervention between three case groups receiving 50, 100 and 150 of wormwood and control group on male wistar rats.	Hydro-alcoholic Extract of wormwood	(69)
<i>Mentha spicata</i> L.	Improving on feed intake and body weight gain of broiler by the supplementation of different levels of spearmint to the diets.	Dry spearmint in addition to basal diets.	(70)
<i>Olea europaea</i>	1) Administration of indomethacin together with the vegetable oils (corn, olive and sunflower oils) and alpha-tocopherol did not cause a statistically significant gastric damage in rats ($P>0.05$)/ these component improved the levels of antioxidant defense systems in rat stomach tissues against oxidative damage. 2) Contrary to the lowest quercetin content, <i>Hypericum perforatum</i> L., (St. John's Wort) oil extracts (HPE) prepared with olive oil (E2) offered the highest protection against gastric damaging action of cold-restraint stress (CRS).	Olive oil. 2) <i>Hypericum perforatum</i> L., (St. John's Wort) oil extracts with maceration flowers in three different vegetable oils: sunflower (E1), olive (E2) and palm oil (E3).	(71) (72)
<i>Cydonia oblonga</i> Mill.	1) Significant changes in the symptoms of reflux including vomiting, cough, agitation and low appetite on infants with reflux after one month administration of quince extract. 2) No significant differences on reducing gastro-esophageal reflux disease symptoms between Quince syrup group and omeprazole receiving group in all pediatrics age groups.	1) Quince fruit extract. 2) Quince syrup made of water extract of Quince which was obtained from its.	(73) (64)
<i>Malus domestica</i> Borkh.	Protective effect of apple against gastrointestinal damage in rats treated with indomethacin/anti-inflammatory effects by preventing neutrophil infiltration in the mucosa.	Apple peel polyphenol extract.	(74)