Herbal Remedies for Functional Dyspepsia and Traditional Iranian Medicine Perspective

Mahmoud Babaeian, 1 Mohsen Naseri, 2* Mohammad Kamalinejad, 3 Farzaneh Ghaffari, 4 Fatemeh Emadi, 2 Awat Feizi, 5 Nafiseh Hosseini Yekta, 1 and Peyman Adibi 6

1 Department of Iranian Traditional Medicine, Faculty of Medicine, Shahed University, Tehran, IR Iran
2 Traditional Medicin Clinical Trial Research Center, Shahed University, Tehran, IR Iran
3 Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
4 Department of History of Medicine, School of Traditional Medicine, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran
5 Department of Biostatistics and Epidemiology, School of Health, Isfahan University Medical, Isfahan, IR Iran
6 Integrative Functional Gastroenterology Research Center, Isfahan University of Medical Sciences, Isfahan, IR Iran

*Corresponding Author: Mohsen Naseri, Traditional Medicine Clinical Trial Research Center, Shahed University, Tehran, IR Iran. Tel/Fax: +98-2166464320, E-mail: naseri@shahed.ac.ir

Abstract

Context: Functional dyspepsia (FD) is a functional gastro-intestinal disorder with high prevalence. Among various treatment options, treatment by complementary and alternative medicines especially herbal remedies also practiced. Traditional Iranian medicine (TIM), a valuable resource of valid applied studies of ancient Iranian scholars, recommends numerous medicinal plants to treat dyspepsia symptoms. In this study, through investigation of TIM references, we aimed to identify medicinal plants for treatment of digestion insufficiency.

Evidence Acquisition: In this qualitative study, dyspepsia symptoms including fullness, early satiety, bloating, nausea, and belching were checked under reliable sources of traditional medicine. Then medicinal plants recommended for the treatment of the symptoms were extracted from the books. Likewise, for investigating the pharmacological properties of medicinal plants used for the relieving of dyspepsia symptoms, electronic databases such as PubMed, Scopus, Google Scholar and some Iranian databases like SID and IranMedex were employed.

Results: The study yielded 105 plants from 37 families which could treat various dyspepsia symptoms; fifty-seven plants, mainly from Apiaceae, Lamiaceae, Amaryllidaceae and Zingiberaceae had digestive effects. In this research, based on the information in TIM reference texts, we obtained 58 plants effective for bloating, 40 for nausea, 37 for appetite loss and 7 for belching. In human clinical trials conducted on medicinal plants effective for FD symptoms, 7 single plants were used.

Conclusions: Finding the medicinal plants effective on digestion insufficiency based on TIM could suggest a better strategy for the relieving of dyspepsia symptoms. Traditional Iranian medicine prescribes medicinal plants based on each patient's personal characteristics and practices multiple target therapies.

Keywords: Herbal Medicine, Dyspepsia, Medicinal Plants, Medicine, Traditional

1. Context

Functional Dyspepsia (FD) is a Non organic gastro-intestinal disorder causing different symptoms such as fullness, early satiety, bloating and nausea in upper abdomen (1, 2). This common nonlife-threatening disorder with its recurring symptoms needs numerous medical visits, which impose high costs on the society and affect the patients' quality of life (3).

The cause for FD is not known yet, but a number of theories was introduced to provide explanation; delay in emptying the stomach contents, genetic factors, infection with a bacterium called Helicobacter pylori, neurolog ic-hormonal disorders, autonomic disorders, stress and mental disorders, visceral hypersensitivity, and alteration of duodenum sensitivity to acids and lipids are some speculated causes (1).

A number of medicinal and non-medicinal treatments have been suggested; most of these fail to cure patients completely and mainly focus on relieving the symptoms. The medicinal treatments used to date include acid suppressing medicines like proton pump inhibitors, H2-blockers, and simethicone, motility affecting drugs such as mosapride, domperidone, erythromycin, anti-depressants, Selective Serotonin re-uptake inhibitors (SSRIs) and medicinal plants (4).

In recent years, herbal treatments in general and for FD in particular have received increasing attention. To treat...
FD symptoms, various plants have been examined. Most of the medicines obtained this way are combinations of several plants from studies of traditional medicine in different countries (4).

Iranian Traditional medicine (TIM) with a concentration on temperament and humors is a valuable resource of carefully conducted applied studies of medical scientists and scholars of Iran in the course of history. These studies have passed on to us in the form of medical prescriptions for prevention, diagnosis, and treatment of health conditions (5).

One of the realms TIM has tackled is digestive disorders and an important disease often discussed in TIM is digestion insufficiency (za‘f-ol-hazm) (6, 7). In TIM, digestion insufficiency is defined so: “Digestive insufficiency is when food does not leave stomach in time and the stay exceeds usual time, which entails symptoms such as stomach fullness, nausea, belching, and bloating” (7).

From TIM perspective, treatment of digestion disorders includes lifestyle modification, drug therapy, and nondrug techniques such as massage (Dalk) and reflex therapy (Ghamz). Either during lifestyle modification period (particularly modification of physical activity, eating habits, and sleep habits) or after it, treatment with medicinal plants is practiced (6, 8).

In this study, through investigation of TIM references, we aimed to identify medicinal plants for treatment of digestion insufficiency and provide a coherent account of how TIM deals with digestion insufficiency.

2. Evidence Acquisition

In this qualitative study, traditional medicine reference books from various historical eras, such as The Canon of Medicine by Avicenna (10th and 11th centuries) (6), Sharh-ol-Asbabval Alamat by Nafis-ebne-avaz-e-Kermani (15th century) (7), Tohfat-ol-Momenin by Hakim Momen Husseini (17th century) (9) and Makhzan-Al’Advieh by Hakim Aghili Khorsan (18th century) (10) were firstly selected after consulting the team of authors.

To find matches for old names in modern scientific classification, two botany references (11, 12) and electronic databases such as United States Department of Agriculture (USDA) and the plantlist.org suggested by the research team were used.

To investigate the pharmacological properties of medicinal plants used in clinical trials for the relief of dyspepsia symptoms, electronic databases like PubMed, Scopus, Google Scholar and some Iranian databases like SID and IranMedex were employed.

Data collected from TIM books and modern sources, like names and pharmacological properties were submitted to research team; thus, all authors were involved in the process of analysis.

After selecting search references, dyspepsia symptoms including fullness, early satiation, bloating, belching, and nausea were firstly checked under their equal items in TIM references. Then, effective drugs were searched in TIM sources by fullness (Seql-e-meda), early satiety (Noqsan-e-shahvat-a-ta’am), bloating (Naftkh-e-me’di), belching (Aroq), nausea (Tahavo) and digestion insufficiency (za‘f-ol-hazm).

To study the properties of medicinal plants in clinical trials, key words such as nonulcer dyspepsia, dyspepsia, functional dyspepsia, the plants’ scientific names, and their pharmacological properties were used.

3. Results

After finding matches between main symptoms of dyspepsia (fullness, early satiety, bloating, belching, and nausea) and symptoms mentioned in TIM references and later, searching effective plants for these symptoms, we obtained 105 plants from 37 plant families effective for relieving dyspepsia symptoms. Most plants belonged to Apiaceae (14 plants), Lamiaceae (11 plants), Rosaceae (8 plants), Compositae (7 plants), Amaryllidaceae (6 plants), Rutaceae (5 plants), Zingiberaceae (5 plants), Anacardiaceae (4 plants), Brassicaceae (4 plants), Piperaceae (4 plants), respectively (Table 1).

| Scientific Name | Family | Common Name | Parts Used | Stomach-Strengthening Characteristics From the TIM Perspective | Effective in Dyspepsia Symptoms | EI |
|-----------------|--------|-------------|------------|------------------------------------------------------------|-------------------------------|-----|
| Acorus calamus L. | Acoraceae | Calamus | Rhizome | * | * | * | * | * | * |
| Allium cepa L. | Amaryllidaceae | Onion | Bulb | * | * | * | * | * | * |
| Allium hirtifolium Boiss. | Amaryllidaceae | Persian shallot | Bulb | * | * | * | * | * | * |
| Allium ampeloprasum L. | Amaryllidaceae | wild leek | Leaf, root | * | * | * | * | * | * |
| Allium Sativum L. | Amaryllidaceae | Garlic | Bulb | * | * | * | * | * | * |
| Pistacia atlantica Desf. | Anacardiaceae | Chio Gum | Gum | * | * | * | * | * | * |
| Pistacia lenticus Desf. | Anacardiaceae | Mastic tree | Oleogum Resin | * | * | * | * | * | * |
| Common Name                  | Family         | Additional Information          | Part(s) | Note(s) |
|------------------------------|----------------|---------------------------------|---------|---------|
| Pistacia vera L.             | Anacardiaceae  | Pistachio Rind                   | *       | *       | *       |
| Rhus coriaria L.             | Anacardiaceae  | Sumac Fruit                      | *       | *       | *       |
| Anethum graveolens L.        | Apiaceae       | Dill Leaf, seed                  | *       | *       |         |
| Apium graveolens L.          | Apiaceae       | Celery Herb, seed               | *       | *       | *       |
| Bunium persicum (Boiss.) B.Fedtsch | Apiaceae    | Wild Caraway                    | *       | *       | *       |
| Coriandrum sativum L.        | Apiaceae       | Coriander Leaf, seed            | *       | *       |         |
| Cuminum cyminum L.           | Apiaceae       | Common Fennel                    | *       | *       | *       |
| Daucus carota L.             | Apiaceae       | Carrot Seed, root               |         | *       |         |
| Eryngium caeruleum M.Bieb.   | Apiaceae       | Eryngo Herb                     | *       | *       | *       |
| Falcaria vulgaris Bernh.     | Apiaceae       | Common Falcaria                 | *       | *       |         |
| Ferula asafoetida L.         | Apiaceae       | Aassa-Foetida Gum               | *       | *       | *       |
| Ferulago lagunata (Schltdl.) Boiss | Apiaceae    | Ferulago Fruit                  | *       | *       | *       |
| Foeniculum vulgare Mill.     | Apiaceae       | Fennel Fruit                    |         | *       |         |
| Petroselinum crispum (Mill.) Fuss | Apiaceae    | Parsley Seed                    | *       | *       |         |
| Pimpinella anisum L.         | Apiaceae       | Anise Fruit                     | *       | *       |         |
| Trachyspermum ammi (L.) Sprague | Apiaceae    | Bishop’s Weed Fruit             | *       | *       | *       |
| Asparagus officinalis L.     | Asparagaceae   | Common asparagus                | *       | *       |         |
| Crinium maritima (L.) Stearn | Asparagaceae   | Squill Bulb                     | *       | *       |         |
| Berberis vulgaris L.         | Berberidaceae  | Barberry Fruit                  |         | *       |         |
| Asperugo procumbens L. b     | Boraginaceae   | German Madwort                  | *       | *       |         |
| Brassica nigra (L.) K.Koch   | Brassicaceae   | Black mustard                   | *       | *       |         |
| Descarainia sophia (L.) Webb ex Prantl | Brassicaceae | Flixweed Seed                  | *       | *       |         |
| Lepidium sativum L.          | Brassicaceae   | garden cress                    | *       | *       |         |
| Raphanus raphanistrum subsp. sativus L. Domin | Brassicaceae | Black radish                   | *       | *       |         |
| Boswellia sacra Flueck.      | Burseraceae    | Oliban oleogum resin            | *       | *       |         |
| Commiphora myrrha (Nees) Engl. | Burseraceae   | Common myrrh Gum                | *       |       |         |
| Commiphora gileadensis (L.) C.Chr. | Burseraceae | Balessan Bark, seed             | *       | *       |         |
| Nardostachys jatamanss (D.Don) DC. | Caprifoliaceae | Indian valerian Root           | *       | *       |         |
| Valeriana sisybriifolia Vahl | Caprifoliaceae | Mountain valerian               | *       | *       |         |
| Terminalia bellirica (Gaertn.) Roxb | Combretaceae | bastard myrobalan Fruit        | *       | *       |         |
| Terminalia chebula Retz.     | Combretaceae   | Myrobalan Fruit                 | *       | *       |         |
| Artemisia absinthium L.      | Compositae     | Wormwood Herb                   | *       | *       | *       |
| Cichorium intybus L.         | Compositae     | Chicory Herb                    | *       | *       |         |
| Doreonicum paradoxanum L.    | Compositae     | Leopards-bane Root              | *       | *       | *       |
| Gandella tournefortii L.     | Compositae     | Galgal Leaf, flower             | *       | *       |         |
| Inula helenium L.            | Compositae     | Elecampane Rhizome              | *       | *       | *       |
| Lactuca sativa L.            | Compositae     | Lettuce Herb, seed              | *       | *       |         |
| Tanacetum balsamita L.       | Compositae     | Costmary Leaf                   | *       | *       | *       |
| Scientific Name                      | Family         | Common Name                      | Part(s)        | Notes               |
|-------------------------------------|----------------|----------------------------------|----------------|---------------------|
| Cuscuta epithymum (L.) L.            | Convolvulaceae | Clover dodder                     | Herb           |                     |
| Juniperus oxycedrus L.              | Cupressaceae   | Western Prickly Juniper          | Fruit, Bark    |                     |
| Cyperus rotundus L.                 | Cyperaceae     | Nutsedges                        | Root           |                     |
| Elaeagnus angustifolia L.           | Elaeagnaceae   | Oleaster                         | Flower         |                     |
| Dracunculus multicaule Montbret and Aucher ex Benth. | Lamiaceae | Dragonhead                       | Herb           |                     |
| Melisa officinalis L. b             | Lamiaceae      | Balm                             | Herb           |                     |
| Mentha longifolia (L.) L.           | Lamiaceae      | Wild mint                        | Herb           |                     |
| Mentha spicata L.                   | Lamiaceae      | Mint                             | Leaf           |                     |
| Hyssopus officinalis L.             | Lamiaceae      | Hyssop                           | Flower         |                     |
| Ocimum basilicum L.                 | Lamiaceae      | Basil                            | Leaf           |                     |
| Salvia macrosiphon Boiss.           | Lamiaceae      | Wild sage seeds                  | Seed           |                     |
| Satureja hortensis L.               | Lamiaceae      | Summer savory                    | Herb, seed     |                     |
| Stachys lavandulifolia Vahl         | Lamiaceae      | Betony                           | Flower         |                     |
| Teucrium polium L.                  | Lamiaceae      | Poleymander                       | Leaf, flower   |                     |
| Ziziphus clinopodioides Lam.        | Lamiaceae      | Wild Thyme                       | Herb           |                     |
| Cinnamomum cassia (L.) J. Presl     | Lauraceae      | Cassia                           | Bark           |                     |
| Cinnamomum verum J. Presl           | Lauraceae      | Cinnamom                        | Bark           |                     |
| Caesalpinia bonduc (L.) Roxb        | Leguminosae    | Nicker tree                      | Fruit          |                     |
| Glycyrrhiza glabra L.               | Leguminosae    | Licorice                         | Rhizome        |                     |
| Lupinus albus L.                    | Leguminosae    | Yellow Lupine                    | Seed           |                     |
| Tamarindus indica L.                | Leguminosae    | Tamarind                         | Fruit pulp     |                     |
| Myristica fragrans Houtt.           | Myristicaceae  | Nutmeg                           | Fruit          |                     |
| Myrtus communis L.                  | Myrtaceae      | Myrtle                           | Leaf, fruit    |                     |
| Syzygium aromaticum (L.) Merr. and L.M.Perry | Myrtaceae | Clove                            | Bud            |                     |
| Chelidonium majus L.                | Papaveraceae   | Greater celandine                | Rhizome        |                     |
| Phyllanthus emblica L.              | Phyllanthaceae | Indian gooseberry                | Fruit          |                     |
| Piper betle L.                      | Piperaceae     | Betel nut                        | Leaf           |                     |
| Piper cubeba L. C                   | Piperaceae     | Cubebes                          | Fruit          |                     |
| Piper longum L.                     | Piperaceae     | Long pepper                      | Fruit          |                     |
| Piper nigrum L.                     | Piperaceae     | Black pepper                     | Fruit          |                     |
| Bambusa bambos (L.) Voss            | Poaceae        | Golden Bamboo                    | Secretions     |                     |
| Cymbopogon jwarancusa subsp. Olivierii (Boiss.) Soenarko | Poaceae | Lemongrass                      | Root, bud      |                     |
| Cynodon dactylon (L.) Pers.         | Poaceae        | Bermudagrassroot                 | Rhizome        |                     |
| Persicaria hydropiper (L.) Delarbre  | Polygonaceae   | Water-pepper                     | Seed           |                     |
| Rheum ribes L.                      | Polygonaceae   | Rhubarb                          | Root           |                     |
| Rumex conglomeratus Murray          | Polygonaceae   | clustered dock                   | Fruit          |                     |
| Portulaca oleracea L.               | Portulacaceae  | Common Purslane                  | Seed           |                     |
| Nigella sativa L.                   | Ranunculaceae  | black cumin                      | Seed           |                     |
Seventy-eight plants were endemic in Iran. Some plants like green tea were not originally in Iran but had been grown in recent centuries. Plants from Zingiberaceae, Combretaceae, Burseraceae, Piperaceae, Poaceae groups are imported to Iran. Fifty-seven plants mainly from Apiaceae, Lamiaceae, Amaryllidaceae, Zingiberaceae groups were effective for digestion insufficiency. Fifty-eight plants mainly from Lamiaceae, Zingiberaceae, Compositae, Apiaceae families were effective for bloating. Forty plants effective for nausea were from Rosaceae, Apiaceae, Lamiaceae, Zingiberaceae, Rutaceae groups. Thirty-seven plants from Rosaceae and Rutaceae, Apiaceae, Lamiaceae families had appetite-increasing features (Table 1).

According to TIM viewpoint, from those plants effective for different symptoms of dyspepsia, 68 plants had stomach-strengthening characteristics.

3.1. Modern Evidence for the Efficacy of Some Medicinal Plants in Traditional Iranian Medicine Used for the Treatment of Dyspepsia

The systematic review conducted by Thompson coon and Ernst yielded 44 plants effective for FD symptoms (13). The effectiveness of seven of these medicinal plants which we have described in Table 1 has been confirmed in the mentioned study (Table 2).

Some recent evidences for dyspepsia concerning these 7 plants are made as follows:

3.1.1. Chelidonium majus

Greater celandine is a member of the Papaveraceae family, which is called Mamiran in TIM. From the viewpoint of TIM, the rhizome of celandine is carminative,
antidiarrheal and analgesic properties. Greater Celandine contains at least 20 different alkaloids which have anti-spasmodytic action on smooth muscles and also stimulate bile flow. This medicinal plant has antiviral, antibacterial, and anti-inflammatory properties (21, 22). However, the ingestion of celandine can lead to a chronic hepatitis and fibrosis (22).

3.1.2. *Glycyrrhiza glabra* L.

The rhizome of Licorice from Leguminosae family is called Shirinbayan in TIM. According to TIM, Licorice has brain strengthening characteristics, carminative, analgesic and scavenging properties. Research has shown that besides anti-inflammatory and analgesic features Licorice is also enhancing gastric mucus secretion and anti-ulcer activity, anti-*Helicobacter pylori* (16, 24). Black seed and derived thymoquinone have been shown to modulate prostaglandins and leukotrienes production (24).

3.1.3. *Nigella sativa* L.

The seed of black cumin from Ranunculaceae family is called Siyah-dane in TIM. This plant, according to TIM, is recommended for infection, inflammation, and gastrointestinal problems such as nausea, flatulence, dysentery, and diarrhea. Research has shown that besides anti-inflammatory and immune system features, black cumin is antibacterial (against a wide range of organisms such as *Helicobacter pylori*), histamine release inhibitor, and the gastric anti-secretory, anti-ulcer activities (16, 24). Black seed and derived thymoquinone have been shown to modulate prostaglandins and leukotrienes production (24).

3.1.4. *Ocimum basilicum* L.

The leaf of Basil (*Ocimum basilicum* L.) from Lamiaceae family is called rehan in TIM. This plant, according to TIM, strengthens stomach, nervous system and is also carminative. Basil has the anti-inflammatory, antibacterial activities and also has been demonstrated to decrease acid and pepsin outputs (17, 25).

3.1.5. *Phyllanthus emblica* L.

The fruit of Amla (*Phyllanthus emblica* L.) is from Phyllanthaceae family. This plant, according to TIM, strengthens heart, nervous system and stomach and is an astringent medicinal plant, anti-nausea and appetite increasing plant. In addition to antibacterial, anti-cancerous, anti-inflammatory effects (26), this medicinal plant also has cytoprotective acid-reducing features (18).

3.1.6. *Pistacia lenticus* Desf.

A commonly prescribed medicinal plant in TIM is Mas-
tic Gum (Pistacia lenticus Desf.) called Mastaki. It is known to positively affect brain, kidney, heart, and liver functions and is also effective for gastrointestinal problems particularly digestion disorder. Research indicates that Mustic Gum acts against different microorganisms specially Helicobacter pylori (19), urease activity and also has inflammatory features especially against Prostaglandin E2 and Nitric oxide (27, 28). In addition, it is a potent radical scavenging substance (28).

3.17. Zingiber officinale Roscoe

One medicinal plant used for FD treatment is rhizome of Ginger (Zingiber officinale Roscoe) which is called Zanjebil in TIM. According to TIM, this plant is stomach tonic and is effective for digestion problems, bloating, and nausea. Pharmacologically, this plant has free radical scavenging, antioxidant, antiulcer, antibacterial, antisapmodic and anti-inflammatory features (29, 30).

Hu et al. in their study on the effect of ginger on gastric motility showed that this plant increased the speed of gastric motility and gastric emptying more than the placebo. These effects could potentially be beneficial in symptomatic patient groups (20).

3.2. Traditional Iranian Medicine and Dyspepsia

Dyspepsia is with a wide range of symptoms that occurs in upper abdomen. In TIM, digestion insufficiency is seen as one of the stomach diseases. According to TIM, stomach plays an important role in gastric digestion (31).

Various digestive insufficiency causes have been suggested in TIM. These could be classified into two main groups of internal and external causes. Some examples of internal causes are congenital causes like a small size stomach, insufficiency of stomach tissue, stomach ulcer and inflammation, liver disorder, brain disorder, inefficient abdominal membrane lining, and stomach malfunction. Examples of external causes are wrong eating habits, air pollution, unhealthful drinking water, chronic mental disorders, and inappropriate posture or body movements (6, 7, 32).

From TIM perspective, medicinal plants affect pathophysiological causes of digestion disorder in a number of ways. Two major mechanisms are increased temperature in the stomach and facility of gastric motility.

Other mechanisms effective for dyspepsia symptoms in TIM are waste removal and stomach strengthening. From TIM perspectives, nourishing medicinal plants are those which both help remove waste from stomach and also strengthen its tissue against penetration of harmful substances. This could be done through increased gastric motility or the astringent features of the medicinal plant.

By TIM, certain medicinal plants help treat symptoms of dyspepsia due to their pain relieving characteristics. An example of such plants which is both pharmacologically and clinically tested is Mint (Mentha spicata L.) from Labiatae family. By TIM, mint induces a feeling of happiness, strengthens stomach, removes waste, relieves pain and treats digestion disorder. Research has shown that besides anti-bacterial, anti-depressive, anti-soporific and analgesic features (33), mint is also antisapmodic. It seems peppermint oil with its calcium influx blocking feature can treat bloating through its antisapmodic effect on smooth muscles of digestive tract (13, 34).

Certain medicinal plants help relieve dyspepsia symptoms via their antidepressant properties. One example is Limon balm (Melissa officinalis L.) from Labiatae family. The leaf of this plant which is called Badranj buye in TIM has antidepressant and sedative features besides anti-inflammatory and radical scavenging properties (35).

4. Conclusions

Since pathophysiological causes for FD symptoms are varied, there seems to be no single treatment for all patients. Treatment with medicinal plants has attracted the attention of scientists in many countries. Traditional Iranian medicine has paid a great deal of attention to digestive disorders and particularly to digestion insufficiency. Regarding current evidence, it seems that TIM has always prescribed medicinal plants based on their characteristics and the patient’s condition. In addition to digestive effects, these plants have had other effects such as effects on brain, cardiovascular, and liver functions. It appears that medicinal plants effective for digestion problem have been used to target more than one dyspepsia problem. Often to achieve multiple target therapies, combinations of medicinal plants have been used in TIM. The followings are the expected effects of medicinal plants in TIM:

They should increase gastric temperature necessary for gastric digestion, remove waste from stomach, relieve pain and bloating, increase gastric motility, be astringent, strengthen brain and cardio-vascular functions, and have sedative effects.

An awareness of various features and functional mechanisms of medicinal plants in treating FD symptoms, in addition to discovery of new medicinal products, will provide physicians with more reliable medicinal options at their disposal for the treatment of these patients who often are suffering from mental disorders, too.

This study is a great report of medicinal plants mention in TIM texts for digestive problems. Finding the medicinal plants effective on digestion insufficiency based on TIM could suggest a better strategy for relieving dyspepsia symptoms. Due to lack of enough papers and review articles on TIM viewpoints, searching was difficult.

Acknowledgments

This study is a part of a PhD thesis entitled: Explanation of Etiologies and Clinical Manifestations of Dyspepsia According to Traditional Iranian Medicine (Department of Traditional Medicine, Shahed University, Tehran, IR Iran).
Footnote

Authors’ Contributions: Mahmoud Babaeian contributed in grant writing, data gathering, and drafting of the manuscript; Mohsen Naseri contributed in study design, revising the draft and interpretation; Fatemeh Emadi, Mohammad Kamalinejad and Nafiseh Hosseini Yekt contributed in data gathering and revision of final version of manuscript. Farzaneh Ghaffari, Awat Feizi and Peyman Adibi contributed toward the guidance, revision, and correction of the manuscript.

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