

# Review of an Aloe-Based Formulation Used in Iranian Traditional Medicine

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## Abstract

**Context:** In Iranian traditional medicine (ITM), purgation is a simple and effective way of removing waste humors from the body. Purgation not only increases peristaltic movements in the gastrointestinal system but also relieves many symptoms that arise due to the retention of waste humors in the body's organs. The aim of the present study is to introduce one of the most important Aloe-based purgative medications used in ITM: *Ayarij-e-Faiqra*.

**Evidence Acquisition:** The main Iranian medical and pharmaceutical text books, composed between the 9th and 19th centuries, were searched for key words related to *Ayarij* and *Faiqra*. All references to and formulations of *Ayarij-e-Faiqra* were reviewed. Then, scientific databases, including Web of Knowledge, Science Direct, PubMed, and Google Scholar were searched for references to the biological effects of the plants used in *Ayarij-e-Faiqra* formulations.

**Results:** *Ayarij* is the common name for medicines that contain a purgative agent as the main constituent. Other ingredients are often added to improve efficacy and reduce side effects, or to allow the medicine to function as a delivering agent. Aloe is the main constituent of *Ayarij-e-Faiqra*. It has a wide range of indications and an important role in balancing the body's humors in ITM. It can be used, therefore, in the treatment of various diseases. The prescriptions given differ across the manuscripts studied, with some formulations having been used more often, although the instructions for administration and dosage tend to differ.

**Conclusions:** In both ITM and modern medicine, *Ayarij-e-Faiqra* is a powerful purgative medicine because *Aloe* spp. dried juice is the main ingredient. This juice has been used with other components to increase the efficacy of the medicine and to reduce the adverse effects associated with *Ayarij-e-Faiqra*. In ITM, purgative medicine expels and eliminates waste humors from body systems. In modern medicine, most studies focus on the polysaccharide constituent of *Aloe* spp. gel (not the juice), and although data about the modifying effects of each separate ingredient in *Ayarij-e-Faiqra* can be found, more studies are required that analyze all the ingredients in *Aloe* spp. dried juice in order to give a complete medical profile for *Ayarij-e-Faiqra*.

**Keywords:** Aloe, Purgative, Iranian Traditional Medicine, *Ayarij-e-Faiqra*

## 1. Context

In spite of the progress being made in patient treatment and the new scientific technologies being used to promote patient health, a significant percentage of patients still have faith in complementary and alternative medicine (CAM), especially where chronic diseases are concerned, given the lack of effectiveness, the cost, and the side effects associated with synthetic drugs. Iranian traditional medicine (ITM) is one of the oldest and richest traditional systems of medicine, which has been developed and improved over many centuries. It reached its summit in Avicenna's time, in the 10th century (980 - 1037 AD) (1). In ITM, a holistic approach is taken to the prevention of diseases. Promotion of a healthy lifestyle is preferable to treat-

ment. ITM espouses the belief that having balance in the four humors (phlegm, blood, yellow bile, and black bile) establishes a healthy body (2); alterations to this balance are said to result in illness. The human body produces waste humors that are normally expelled from the body through urine, feces, perspiration, sputum, menses (in women), and other bodily secretions. ITM states that any obstruction, occlusion, blockage, or other similar cause can lead to the retention of waste humors. Regulation or elimination of the waste humor in question leads to the rebalancing of the humors and, as ITM believers contend, cures the problem (3, 4). Research into ITM indicates that purgation is one of the simplest and most effective ways of clearing waste humors from the body. This does not mean sim-

ply increasing the number of times one defecates per day or softening impacted feces. In ITM, purgation covers not only the gastrointestinal system, but also other body systems; for example, in Zakhirah-i Kharazm' Shahi (article 1, part 3, chapter 15), laxatives are mentioned as a tool for improving the function of the GI system and are used as a treatment for constipation, but it is also said that purgation (via a systemic agent) expels waste humors from vessels, membranes, and all parts of the body. Since the nature of the elimination of waste humors varies for different organs, ancient ITM physicians used many kinds of purgative medicines, which had specific effects on particular organs (5). In The Canon of MEDICINE (volume 1, part 4), Avicenna discusses "various modes of treatment with regard to general diseases" and describes "different kinds of purgatives" (section 9). He believed that there were four main mechanisms related to purgative medicines: 1) dissolving the humor *Tahlil*, 2) squeezing the intestines (*ASr*), 3) softening the material *Taleein*, and 4) producing mucilage (*Izlagh*) (4).

One of the most common purgative medicines with multiple indications in ITM is Ayarij, which includes a purgative agent as the main constituent, alongside several other ingredients. The ingredients in "Ayarij" formulations have been described as having several functions, such as: 1) improving the efficacy of the formulation and 2) decreasing side effects. It should be taken into consideration, however, that multi-gradient formulations tend to be mentioned as single medicines in ITM literature and it is essential, therefore, to conduct more research to clarify the role of each component in such formulations (4-7). Moreover, there are different kinds of Ayarij mentioned in ITM literature. The Faiqra formulation discussed here (Faiqra meaning "bitter taste") is the most commonly discussed variety of Ayarij in ITM textbooks. It has been used for the treatment of many diseases and its main constituent, Aloe spp. dried juice, is a purgative agent (4, 5, 7). Botanists who have tried to establish which herbs are mentioned in ITM believe that Aloe spp. dried juice is equal to the material called shirabe sabre zard in ITM literature, which is a purgative substance (8-10). The Aloe genus belongs to the Asphodelaceae family (formerly the Liliaceae family), which has nearly 420 species. The term "aloe" is derived from the Arabic word *alloeh*, which means a glowing, bitter substance. *Aloe vera* is cultivated in many regions in Iran, and *A. littoralis* grows wild in several areas of the country - especially the southern provinces and on the Persian Gulf islands (11-13). The history of Aloe usage as a therapeutic agent, as well as a component in cosmetics, dates back to ancient times. Traditionally, *Aloe* spp. dried juice was the main medicinal agent used in most treatments from the time of the Roman Empire onwards. Aloe spp.

dried juice had been prescribed on the Arabian Peninsula in small doses as a tonic thought to improve digestion. In higher doses, it is useful as a purgative agent and as an emmenagogue. Given its high degree of biodiversity, it is not surprising that numerous traditional healing systems use Aloe in the treatment of many disorders. The herb plays a specific and important role in ITM.

In modern medicine, there are many indications for the use of oral *Aloe* spp. gel, but the dried juice is utilized mainly as a purgative due to the anthraquinones and pre-anthraquinones it contains (14). Studies have shown that the leaf pulp and liquid fraction of *Aloe* spp. act against various microorganisms (15). The ethanol extract therein has also been shown to cause significant, dose-dependent increases in total white-blood-cell counts and macrophages (16). In acute gastric mucosal lesions, the extract has been used to inhibit gastric acid secretion and provide gastro protection (17). A new study has shown that processed *Aloe* spp. gel lowers not only blood glucose levels (by decreasing insulin resistance), but also triglyceride levels in the livers and plasma of mice (18). There is also some evidence to suggest that Aloe gel has the same healing effects on the mucous membranes of the digestive tract as it has on external wounds. *Aloe* spp. dried juice creates an effect called the "bitter tonic effect"; the bitter taste stimulates the Vagus and then increases the secretion of gastric juices, thus improving digestion. The bitter substance acts as a cardio-tonic medicine (19). The purgative action of *Aloe* spp. dried juice is also well known. Other biological activities related to Aloe are more complicated and are under study. The main objective of the present study is to review the roles and formulations of *Ayarij-e-Faiqra* in ITM literature and modern references to the formulation. Such research can be used to rationalize and justify the use of the formulations present in traditional medicine in the development of phytomedicine.

## 2. Evidence Acquisition

When searching for *Ayarij-e-Faiqra* in ITM textbooks, the main available Iranian medical and pharmaceutical manuscripts composed between the 9th and 19th centuries AD were used. These texts are utilized as references on the Iranian PhD program in traditional pharmacy and include Ferdos-al-Hekmah fi Tib, Al-Havi, The Canon of Medicine, Mojarabat Hakim Gilani, Menhaj ol Bayan, Zakhirah-i Khvarazm'Shahi, Al- Aghraz Tebbieh, Qarabadin-e-Ghalanasy, Almokhtarat fi Tib, Menhaj ol Dokan, Alomdeh fi Jerahat, Qarabadin-e-Shafaei, Tohfah ol Momenin, Tibb-e-Akbari, Qarabadin-e-Salehi, Qarabadin-e-Kabir, and Exir Azam. These texts were searched for the key words Ayarij and Faiqra in both Arabic and Persian.

The traditional names of the species were also matched to the scientific names using botanical text references (8, 10, 20, 21). Then, in order to find possible evidence of the efficacy of Ayarij, electronic science databases including Web of Knowledge, Science Direct, PubMed, and Google Scholar were searched for references to each of the plants used in *Ayarij-e-Faiqra* prescriptions, as well as the words "Aloe," "Iyarij," "Iyaraj," "Ayarij," "Aitaraj," "bitter aperients," "Faiqara," "Faiqra," "Feqra," "Fighra," and "Fyqra," up to April 2016.

### 3. Results

*Ayarij* means "divine medicine" (4-7), a term which came from Hippocrates' secret prescriptions. It was used in different forms by royal families only for thousands of years before the time of Hippocrates (6). There are six main kinds of *Ayarij* mentioned in ITM books, which are differentiated based on their components: *Rufus*, *Faiqra*, *Lughazia*, *Arhegenes*, *Galen*, and *Andarukhus* (4, 5, 7). *Ayarij-e-Faiqra* is one of the most important. Types of *Ayarij* and is used for different disorders, appearing in several formulations.

#### 3.1. Ingredients in *Ayarij-e-Faiqra*

The main ingredient in *Ayarij-e-Faiqra* is *Aloe* spp. dried juice, which appears either in an equal amount to, or double the amount of, all the other ingredients in the formulation. Different formulations were found when searching for ITM references. Some herbs were used more frequently in prescriptions than others, including *Pistacia lentiscus*, *Cinnamomum zeylanicum*, *Cinnamomum cassia*, *Nardostachys jatamansi*, *Asarum europaeum*, *Commiphora opobalsamum*, *Crocus sativus*, and *Rosa damascena*. Meanwhile, *Andropogonshoenthus*, *Laurus nobilis*, *Costus speciosus*, *Dianthus barbatus*, *Myristica fragrans*, *Agrimonia eupatoria*, *Gentiana lutea*, *Fumaria officinalis*, *Pimpinella anisum*, *Teucrium polium*, *Artemisia absinthium*, *Lavandula angustifolia*, *Pistacia terebinthus*, *Commiphora mukul*, and *Commiphora myrrha* were mentioned less in the references. Five formulations are repeated the most in the prescriptions found in the literature. The first formula contains one part each of *Pistacia lentiscus*, *Cinnamomum zeylanicum*, *Cinnamomum cassia*, *Nardostachys jatamansi*, *Commiphora opobalsamum* (twig and fruit), *Asarum europaeum*, and *Crocus sativus*, and sixteen parts of *Aloe* spp. dried juice. The second formula is based on the components but the proportion of *Aloe* is reduced by two parts. The third formula is similar to the first but *Crocus sativus* is replaced with *Rosa damascena*. In the fourth formula, *Commiphora opobalsamum* (twig) has been eliminated. The fifth formula is the same as fourth formula but contains half the amount of

*Aloe* spp. dried juice. In three of these five most-repeated formulations, the amount of *Aloe* spp. dried juice is two thirds of the total ingredients; in the other two formulations, the amount of *Aloe* spp. dried juice is equal to the sum of the other ingredients (4, 6, 7, 9, 22-26). All of these formulations have the general effect of expelling and eliminating waste humors, but some of the changes in the formulations can be attributed to the geographical availability of ingredients, historical development, patient tolerance, and the severity of disease.

In some cases, the additive components were changed, based on the condition of the patients or the existence of other diseases; for example, *Crocus sativus* would be replaced with *Rosa damascena* in patients with warm humor headaches, vomiting, or nausea. The type and percentage of the ingredients is also different in some references. Table 1 shows the names, temperaments, parts used, and biological effects of the most frequent ingredients found in *Ayarij-e-Faiqra* in recent studies.

#### 3.2. Indications for *Ayarij-e-Faiqra* in ITM

According to ITM, *Ayarij-e-Faiqra* expels and eliminates waste humors (especially the cold humor and phlegm) from the organs (4-7, 25). It has been used for diverse diseases that affect different organs, as shown in Table 2.

#### 3.3. Routes of Administration

Although *Ayarij-e-Faiqra* was described as being applied orally in most references, the method of administration was through gargling or via nasal drops in a few manuscripts (4, 7, 22-25, 52, 53).

#### 3.4. Dosage Forms

In most traditional references, the method for storing *Ayarij-e-Faiqra* was in the form of dry powder in glass bottles. It was suggested that it should be consumed with water and honey, although there were also solid dosage forms made with honey. Moreover, there were some methods for making solid dosage forms with *Apium graveolens* juice, *Foeniculum vulgare* juice, *Commiphora mukul* juice, *golab* (rose water), or honey with *golab* (4, 6, 7, 22, 53, 54).

#### 3.5. Administration and Dosage

There is no agreement in terms of the time of administration in the ITM references. Some physicians advise taking it before meals on an empty stomach, while others recommend it is taken after meals or even before bed time. In addition, some references advise the use of *Cuscuta epithymum* and *Vitis vinifera* seedless fruits or *Althea officinalis* and *Malva rotundifolia* seeds as forms of decoction to be taken along with the remedy (4-7, 24, 25, 55, 56). The preferred

**Table 1.** The Most Frequently used Ingredients in *Ayarij-e-Faiqra* Formulations in ITM

No.	Scientific Name	Family	Common Name	Traditional Name	Phonetics	Temperament	Part Used	Biological Effects
1	<i>Aloe</i> spp.	Liliaceae	Bitter Aloe	Sabr	/sæbr/	Hot and dry	Leaf extract	Purgative (27), laxative (28-31)
2	<i>Pistacia lentiscus</i> L.	Anacardiaceae	Mastic tree, Lentisk pistache	Mastaki	/mæstæki:/	Hot and dry	Oleo gum resin	Anti-gastric ulcer (32), anti- <i>H. pylori</i> (33)
3	<i>Cinnamomum zeylanicum</i> Blume	Lauraceae	Cinnamon	Darsini	/dɑrsi:ni:/	Hot and dry	Bark	Anti-gastric ulcer (34, 35), anti-inflammatory, wound healing (34-36)
4	<i>Cinnamomum cassia</i> J. Presl	Lauraceae	Cassia, Chinese cinnamon	Salikhah	/sæli:khæh/	Hot and dry	Bark	Antibacterial (human intestinal bacteria) (37), wound healing (38), anti-gastritis and anti-inflammatory (39), antibacterial ( <i>E. coli</i> ) (40)
5	<i>Nardostachys jatamansi</i> DC.	Valerianaceae	Indian Valerian, Spikenard	Sumbul-uttib	/sunbul :tti:b/	Hot and dry	Root	Overcoming depression, anxiety and nervousness (41-44)
6	<i>Commiphora opobalsamum</i> L.	Burseraceae	Balm of Gilead, Balsam of Mecca	Balasan	/bælæsən/	Hot and dry	Aerial part	Anti-gastric ulcer (45), anti-inflammatory (46)
7	<i>Asarum europaeum</i> L.	Aristolochiaceae	Asarabacca	Asaroon	/æsɑru:n/	Hot and dry	Root	Anti-gastric ulcer (47), wound healing (47, 48)
8	<i>Crocus sativus</i> L.	Iridaceae	Saffron	Zafaran	/zæfæɾɔ:n/	Hot and dry	Stigma	Gastro tonic (49)
9	<i>Rosa damascena</i> Mill.	Rosaceae	Damask Rose	Ward	/wærd/	Cold and dry	Flower	Wound healing (50), laxative, anti-inflammatory, (51)

daily dose of *Ayarij-e-Faiqra* was between 4.6 g and 18.2 g. The most frequently recommended daily dose was 6.4 g of the powder, taken with honey and tepid water (4, 6, 7, 23, 25, 52, 57).

### 3.6. Stability

Most *Ayarij* formulations did not have a long shelf life, due mainly to poor packaging. Some methods were applied with a view to extending the shelf life; for example, mixing it with honey could prolong the stability of the medicine (6, 7).

### 3.7. Adverse Reactions

Stomach and kidney disturbances are reported to have occurred due to *Ayarij-e-Faiqra* consumption. *Zizyphus sativa* fruit has been suggested as a substance that can reduce the side effects. ITM scholars also recommend taking warm salty water in the case of the delayed onset of *Ayarij* activation (4, 7, 22, 25).

## 4. Discussion

In modern medicine, purgatives act via several mechanisms: 1) increasing the peristaltic motion of intestine

**Table 2.** Indications for *Ayarij-e-Faiqra* in ITM References<sup>a</sup>

Body System	Indication
<b>Central nervous</b>	Headache, Vertigo, Tinnitus, Bell's palsy, Tremor, Epilepsy, Convulsion, Melancholia, Obsession, Insomnia, Paralysis, Spasm, Amnesia, Dementia, Nightmares
<b>Gastrointestinal</b>	Gastric Ulcer, Vomiting, Diarrhea, Colitis, Constipation, Gastritis, Hepatic Obstruction, Obstructive Jaundice, Worms, Glossitis, Stammer, Hypogeusia, Halitosis
<b>Cardiovascular</b>	Hypotension, Palpitation
<b>Urogenital</b>	Bladder Atony, Dysuria, Renal Stone, Bladder Stone, Bad-smelling Urine
<b>Musculoskeletal</b>	Sciatica, Arthralgia, Lumbago, Gout
<b>Integumentary</b>	Chloasma, Vitiligo, Eczema, Fistula, Wart, Itching, Scabies

<sup>a</sup>We have sought to use the closest English translations for these conditions.

through irritant or stimulant action on the bowel, 2) creating a bulk-forming action on the feces by inhibiting water absorption in the large intestine, 3) softening impacted or hard feces using penetrating water and lipids, 4) lubricating feces to ease the passage through the rectum, 4) the action of osmotic laxatives, 5) Cl-channel activators, 6) opioid receptor antagonists, and 7) 5-HT<sub>4</sub> receptor agonists (58). It seems that *Ayarij-e-Faiqra* induces its effects through increasing the peristaltic motion of the intestine, interaction with water, and electrolyte transportation to the bowels through the *Aloe anthraquinones*, which are the main ingredient (58). As mentioned previously, *Ayarij-e-Faiqra* has a wide range of indications and plays an important role in balancing the body's humors in ITM. It should be noted that, according to ITM, a purgative is not just a treatment for constipation; it is also used to alleviate many symptoms that develop due to the retention of waste humors. *Ayarij-e-Faiqra* could be applied, therefore, even when the GI function is normal (5). An online search for references to the ingredients in *Ayarij-e-Faiqra* indicated that the most frequently used ingredients in *Ayarij-e-Faiqra*, alongside *Aloe* spp. (dried leaf extract), were *Pistacia lentiscus* (dried resin), *Cinnamomum zeylanicum* (dried bark), *Asarum europaeum* (root), *Nardostachys jatamansi* (root), *Commiphora opobalsamum* (twig and fruit), *Cinnamomum cassia* (dried bark), and *Crocus sativus* (dried stigma). These ingredients are used as adjuvants that may improve the efficacy and safety of *Aloe* spp.

In ITM literature, the main reason for using multi-component prescriptions is usually to modify the effects or side effects of the active ingredients. There is no reported toxic interference between the components. Research into the interactions between herbal medicines is in its infancy and we could not find any articles that pointed directly to interference between *Aloe* spp. dried juice and

the other plants in the formulation. There are some studies that mention the toxicity of the aristolochic acid found in *Asarum europaeum*, which has then been eliminated from the formula being used.

Among the additives, *Pistacia lentiscus* tended to be used as a gastro tonic, according to ITM literature. Recent research into gastric and duodenal ulcers in rats has shown, in fact, that mastic, the exudate from *Pistacia lentiscus*, has anti-ulcer properties (32). *Cinnamomum cassia* is added to the formulation to mature the humor and to act as a gastro tonic. It has been mentioned repeatedly as a component in traditional *Ayarij-e-Faiqra* prescriptions. The reason for its use might be explained by its anti-gastritic and anti-inflammatory properties, as confirmed by such studies as that conducted by Yu et al. The anti-inflammatory activity has been shown to occur through the suppression of the Src/Syk-mediated NF- $\kappa$ B activation (39). Compounds derived from the bark of the species have also been shown to exhibit antibacterial activity against human intestinal bacteria (37). Moreover, cinnamic aldehyde obtained from plant shoots has demonstrated inhibitory activity against *Escherichia coli* O157:H7, which is capable of inducing hemorrhagic colitis in human beings (40). These antibacterial effects, along with the anti-inflammatory activity, could be the reasons why *Cinnamomum cassia* tended to be used in the *Ayarij-e-Faiqra* formulation - presumably, it would have been thought to reduce the stomach disturbances and intestinal damage caused by *Ayarij-e-Faiqra*. *Crocus sativus* was also added to the formulation as a gastro tonic, and a recent study into the oral administration of *Crocus sativus* extract has shown that it stimulates gastric secretions in Wistar rats, which could be understood as a confirmation of its gastro-tonic action (49). Regarding other ingredients, *Commiphora opobalsamum* fruits and twigs were also used as gastro tonics and for dispersing humors. The species has been shown to produce anti-ulcer activity and to protect gastric mucosa in different in vivo ulcer models in rats (45). ITM physicians believed that *Nardostachys jatamansi* was a neuro tonic, and many recent in vivo works have commented on the probable effectiveness of the species or its components in overcoming depression, anxiety, and nervousness (41-44, 59). It could be suggested that this component was added to *Ayarij-e-Faiqra* prescriptions in order to decrease patients' agitation and anxiety, thus helping them to be relaxed and more receptive to treatment. *Asarum europaeum* was used in old prescriptions to facilitate purgation and expel humors, but we could not find any similar applications or related recent research that corresponded with the claim. It may be that the toxicity of aristolochic acid (a component of the species) has limited its current usage in research.

It can be suggested that *Ayarij-e-Faiqra* is a suitable purgative medication for the treatment of corresponding diseases in traditional medicine. A review of traditional references to *Ayarij-e-Faiqra* and current research into its ingredients has provided scientific evidence for this matter and highlighted the important of *Ayarij-e-Faiqra* for pharmacological research into the use of traditional treatments for related conditions.

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## Footnotes

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