

## Therapeutic effects of Iranian herbal extracts against *Trichomonas vaginalis*

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### ABSTRACT

*Trichomonas vaginalis* is a flagellated parasite affecting about 276 million people annually worldwide. Trichomoniasis is associated with different complications in pregnant women and infants. 5'-nitroimidazole derivatives (metronidazole, ornidazole, and tinidazole) are FDA approved drugs recommended for trichomoniasis treatment. Treatment with metronidazole 5'-nitroimidazole derivatives is associated with many side effects, and drug resistance to metronidazole has been reported in some cases. Recently, many attempts have been made to evaluate the effects of plants on causative agents of vaginal infections. In our research, the national and international databases were searched and the effects of various herbal extracts on *T. vaginalis* in Iran were reviewed from 2006 to 2016. In articles investigated, some plants had favorable antitrichomonal effects and needed to be further investigated. All the plant extracts have only been evaluated *in vitro*. Surveys of different articles in this review show that the active ingredients present in different parts of plants, including aerial parts, leaves, flowers, stems, and root can be suitable sources for introducing and developing new antitrichomonal compounds. DOI: 10.18869/acadpub.ibj.21.5.285

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### INTRODUCTION

*Trichomonas vaginalis* is a protozoan parasite and the causative agent of infection in human vagina, prostate gland, and urethra<sup>[1-3]</sup>. *T. vaginalis* is a parasite of the Trichomonadidae family and genus of *Trichomonas*. Morphologically, this parasite is pyriform and occasionally amoeboid form<sup>[3-6]</sup>. Prevalence of trichomoniasis is estimated about 276 million new cases annually worldwide and associated with different complications such as preterm birth, high mortality in infant, and low birth weight<sup>[7-9]</sup>. About 85% of infected women and 77% of infected men with this parasite are asymptomatic. In men, trichomoniasis can be associated with urethral discharge and dysuria. In general, among women, the common sites of infection are vagina, urethra, and endocervix, and clinical features include vaginal

discharge (which is often diffuse, malodorous, and yellow-green), dysuria, itching, pruritis, vulvar irritation, and abdominal pain. Other complications could be infection of the adnexal, endometrium, and Skene's and Bartholin's glands. Trichomoniasis also may cause the increased risks of other sexually transmitted diseases; infection is associated with 1.5–2.7 times greater risks of HIV acquisition and transmission<sup>[10-13]</sup>. Trichomoniasis in women is more common at the age of 16-53. Infection is usually transmitted by sexual contact and restricted to the genital tract. Wet mount examination is the most common method of diagnosis, but *T. vaginalis* infection can also be diagnosed by clinical signs, cultures (TYM, TYI-S-33, dorset, and horse serum), and molecular approaches such as polymerase chain reaction, which is the most sensitive and specific method for the detection of *T. vaginalis*<sup>[14-16]</sup>. The

appropriate treatment for trichomoniasis includes the 5'-nitroimidazole derivatives of which metronidazole and tinidazole are the only efficient FDA approved drugs. Recently, some other drugs have been introduced for the treatment of this disease (Table 1)<sup>[17-29]</sup>. Besides, simultaneous treatment of both sexual partners (female and male) is recommended<sup>[17-20]</sup>. Treatment efficiency depends on the influence of host factors. Nitroimidazole may also be required for the effective treatment of HIV-infected women who are infected with *T. vaginalis*. Drug resistance to metronidazole has been reported in some cases<sup>[30,31]</sup>. In recent years, many attempts have been made for the evaluation of the effects of plants on different microorganisms that cause vaginal infection on *T. vaginalis* in vaginal infection. Nowadays, many studies have been performed in replacing medicinal plants with synthetic drugs<sup>[32-36]</sup>.

Search of electronic databases and journals was performed to find the related data reporting the *in vitro* effects of various plant extracts on *T. vaginalis* in Iran. The international databases, including PubMed, Scirus, ISI Web of Science, Scopus, EMBASE, Science Direct, and Google Scholar, as well as national databases covering Iran Medex, IranDoc, Magiran, and Scientific Information Database (ISC) were searched. These searches limited to articles published between the years 2006 and 2016. The keywords used for the literature search for this review were "*Trichomonas vaginalis*", "medicinal plants", "herbal drug", "plant extract", "anti-trichomonas activity", "*in vitro*", and "Iran".

## Chemical drugs for treatment of trichomoniasis

### *Metronidazole*

Metronidazole is a member of the nitroimidazole family and prevents genetic material synthesis by disrupting the DNA of microorganism cells. Metronidazole is highly active against anaerobic bacteria and anaerobic parasites including *T. vaginalis*<sup>[30,37]</sup>. The pharmacological properties of this drug are suitable, and it is accessible as oral, intravenous, vaginal, and topical forms. After oral administration, it is well absorbed and reached the highest level within 1 to 2 hours after ingestion<sup>[30,37,38]</sup>. This drug is effective against many anaerobic bacteria and parasites. Urinary tract is the prominent way of metronidazole excretion. Anaerobic infections, such as abdominal infections, genital tract infections, septicemia, endocardial infection, bone infections, brain and spinal cord infections, pulmonary infections, cutaneous infections. Before some surgeries, metronidazole is used to prevent secondary infections<sup>[30,37,38]</sup>.

### *Side effects and the problem of metronidazole resistance*

Side effects in systemic metronidazole therapy (in less than 1% of patients) include vomiting, diarrhea, abdominal cramps, headache, drowsiness and fever. Intravenous administration is typically associated with thrombophlebitis. Infrequent side effects consists mouth ulcers, headache, glossitis, dizziness, inflammation of the mouth and lips and dark-colored

**Table 1.** Chemotherapeutic agents against trichomoniasis

Drug name	Medial use	Ref.
Metronidazole	Anti-protozoan (giardiasis, trichomoniasis, and amebiasis)	[17-20]
Tinidazole	Anti-protozoan (amebiasis, giardiasis, and trichomoniasis)	[21,22]
Secnidazole	Anti-protozoan (trichomoniasis and dientamoebiasis)	[21,29]
Ornidazole	Anti-protozoan (trichomoniasis)	[23]
Nimorazole	Anti-protozoan (trichomoniasis and head and neck cancer)	[24]
Nitrothiazole	Anti-protozoan (giardiasis, trichomoniasis, and amebiasis)	[25]
Nitazoxanide	Anti-protozoan (cryptosporidiosis, giardiasis, hymenolepiasis, ascariasis, and resistant Trichomoniasis)	[26,25]
Hamycin	Anti-protozoan (trichomoniasis)	[27]
Paramomycin	Cutaneous leishmaniasis, visceral leishmaniasis, and anti-recurrent <i>T. vaginalis</i>	[28]
Sodium nitrite	Anti-microbial and anti- <i>T. vaginalis</i> resistance to metronidazole (used in traditional medicine)	[29]
Nitrofurantoin	Antimicrobials and anti- <i>T. vaginalis</i>	[29]
Furazolidone	Antibacterial and anti- <i>T. vaginalis</i>	[29]

Ref., references

urine<sup>[17-29,39]</sup>. Irregular and long-term use of the metronidazole has led to drug resistance, which is the most important reason for the treatment failure<sup>[37]</sup>. If there is suspicion of metronidazole resistance, metronidazole susceptibility assay is required as it can help to determine the course of subsequent treatment<sup>[29,40]</sup>. The increase in the prevalence of metronidazole-resistant strains shows a need for development of non-nitroimidazole drugs to combat resistant trichomoniasis. Recently, some studies have been conducted to introduce new drugs against trichomoniasis. The use of herbal medicines has been considered due to fewer side effects. While the synthetic drugs are obtained from non-renewable sources as petrochemicals materials, medicinal plants, are renewable in nature<sup>[30-36,41]</sup>.

### Tinidazole

Tinidazole is antiparasitic drug from the 5-nitro-

imidazole family. This drug is commonly used for treating *T. vaginalis* in America. Compared to metronidazole, tinidazole has longer half-life, higher tissue distribution, and fewer side effects. However, its mechanism of action is similar to metronidazole, and the occurrence of cross-resistance is possible. Studies have shown an incomplete cross-resistance to tinidazole in metronidazole-resistant isolates that can possibly be treated by tinidazole, but the similarity of metabolic pathways in metronidazole and tinidazole causes the rapid spread of resistance to tinidazole. Also, its cost is more than metronidazole; therefore, it cannot be used commonly<sup>[22,42]</sup>.

### Literature review of herbal medicine for treatment of trichomoniasis

Active ingredients of plant extract against *T. vaginalis* are mentioned in Table 2.

**Table 2.** Active ingredients of plant extracts against *T. vaginalis* in Iran (2006-2016)

Botanical name	Active ingredients	Part used
<i>Artemisia aucheri</i> Boiss.	Artemisinin <sup>[43,51]</sup>	Leaves
<i>Zataria multiflora</i> Boiss.	Thymol <sup>[44-47,51]</sup>	Leaves
<i>Myrtus communis</i>	Cineol, tannins, and flavonoids <sup>[48-51]</sup>	Leaves
<i>Allium sativum</i> (garlic)	Organosulfur compound, Allicin, Diallyl disulphide, S-Allyl cysteine, and Diallyl trisulfide <sup>[52,53,56]</sup>	Whole plant
<i>Ferula assa-foetida</i>	Monoterpenoids <sup>[54-56]</sup>	Whole plant
<i>Lavandula angustifolia</i>	Linalool alcohol, Cineol, Camphor, Steroidal ketone, and lavandulol <sup>[57-59]</sup>	Leaves and flowers
<i>Eucalyptus camaldulensis</i>	Terpenoid and phenolic compound <sup>[60,61]</sup>	Leaves
<i>Stachys sylvatica</i>	$\alpha$ -Pinene, $\beta$ -Pinene, germacrene-D, and flavonoids <sup>[62,63]</sup>	Aerial parts
<i>Achillea millefolium</i>	Flavonoids <sup>[64,67]</sup>	whole plant and leaves
<i>Artemisia absinthium</i>	Monoterpene (thujone), absinthen, azulenes, phenolic compounds, Flavonoids <sup>[66,67]</sup>	Leaves
<i>Juglans regia</i>	Tannin and naphthoquinones <sup>[65,67]</sup>	Leaves and twigs
<i>Tanacetum Parthenium</i>	Tannin, lactones, and terpenes <sup>[68,69]</sup>	Leaves
<i>Taxus baccata</i>	Alkaloids (taxines A and B) <sup>[70,71]</sup>	Leaves
<i>Viola odorata</i>	Phenolic, terpenoid, and alkaloid compounds <sup>[72,73]</sup>	Leaves, flowers, and stems
<i>Pelargonium roseum</i>	Geranium, citronellol, mannitol, and ethyl alcohol <sup>[74,75]</sup>	Leaves, flowers, and roots
<i>Verbascum thapsus</i>	Saponins, glycosides, glycosaminoglycans, phenyl ethanol, and verbascoside <sup>[76,77]</sup>	Leaves, flowers, and stems
<i>Allium Cepa</i>	Organosulfur compounds, Allyl sulfides, flavonoids, and flavonols <sup>[78,81]</sup>	Whole plant
<i>Olivaria Decumbens</i> Vent	Tymol, threpenin, and carvacrol <sup>[79]</sup>	Aerial parts
<i>Muscari neglectum</i>	Flavonoid, alkaloid, terpenoid, and steroid <sup>[80,81]</sup>	Flowers

### ***Artemisia aucheri* Boiss, *Zataria multiflora* Boiss, and *Myrtus communis***

These plants are native in Iran and are used in traditional medicine as antiparasitic drugs. *Artemisia aucheri* Boiss contains artemisinin, which has antiparasitic properties<sup>[43]</sup>, and *Zataria multiflora* Boiss contains the high amount of thymol, which has anti-inflammatory, antiseptic and antibacterial effects<sup>[44-47]</sup>. *Myrtus communis* is composed of cineol, tannins and flavonoids, which have antiseptic, antioxidant, antibacterial, antiviral and antifungal activities<sup>[48-50]</sup>. Ziaie *et al.*<sup>[51]</sup> surveyed the effect of alcoholic extract of these three plants on *T. vaginalis* *in vitro*. Their results showed that these extracts have different chemical compositions and special effects that inhibit the growth of *T. vaginalis*. Also, all of them had maximum effect in 0.1% w/v and 4 hours after culture so that after this time no parasites were found alive.

### ***Garlic and Ferula assa-foetida***

*Allium sativum*, is the scientific name of garlic, belongs to onion genus. Garlic is native to Central Asia and has been used over than 7000 years. Garlic is used as anticoagulant, anticold, anti cancer and antiparasite<sup>[52,53]</sup>. *Ferula assa-foetida* is native to the deserts of Iran and mountains of Afghanistan and is commonly cultivated in nearby India. This plant grows in different provinces of Iran such as Khorasan, Sistan and Baluchestan, Kerman, and Fars. *Ferula assa-foetida* is used as a digestion aid, antimicrobial, abortifacient, antidote for opium, remedy for asthma and bronchitis, and fighting influenza<sup>[54,55]</sup>. Sarkari *et al.*<sup>[56]</sup> studied the effect of garlic and *Ferula assa-foetida* extract on the growth and proliferation of *T. vaginalis*. Based on the results of this study, 90% of the parasites were killed one hour after adding *Ferula assa-foetida* extract at the concentration of 2 mg/ml, but only 5% of the parasites survived after 2 hours by adding garlic extract at concentration of 0.1 mg/ml.

### ***Lavandula angustifolia***

*Lavandula* belongs to family Lamiceae and genus Lavanduleae. This plant has traditional application as a sedative as well as an antispasmodic, antiparasitic, antibacterial, antioxidant, anticancer, antiviral, antidepressants and anti-inflammatory remedy<sup>[57,58]</sup>. Investigation of antitrichomonal activity of *Lavandula angustifolia* essential oil *in vitro* was conducted by Ezatpur *et al.*<sup>[59]</sup>. They showed that all concentrations of lavender essential oil have good antitrichomonal effect and reduce the number of parasites; all the parasites were killed 90 minutes after exposure to 0.1% *Lavandula angustifolia* essential oil.

### ***Eucalyptus camaldulensis***

Various biological effects of eucalyptus, including antibacterial, antihyperglycemic, and antioxidant activities have been reported, and it seems that the essential oils of Eucalyptus, containing terpenoid and phenolic compounds, play a major role in its biological activities<sup>[60]</sup>. Effects of various concentration of *Eucalyptus camaldulensis* extracts on *T. vaginalis* parasite in culture medium have been surveyed by Hassani *et al.*<sup>[61]</sup>. The obtained results indicated that *E. camaldulensis* extract had 80% growth inhibition in a concentration of 12.5 mg/ml after 24 h. Alcoholic extract in a concentration of 25 mg/ml showed 100% growth inhibition after 24 h, and ethyl acetate extract had 100% growth inhibition with the minimum concentration of 12.5 mg/ml 24 h after culture. Eventually, water extract in the concentration of 50 mg/ml indicated 80% and 100% growth inhibition after 48 and 72 h, respectively<sup>[61]</sup>.

### ***Stachys sylvatica***

*Stachys* is one of the largest genera in the Lamiaceae plant family. It is a genus of about 300 species and a subfamily of Lamioideae. The distribution of the genus covers Europe, Asia, Africa, Australasia, and North America. This plant grows in different regions of Iran's provinces such as Isfahan, Chaharmahal and Bakhtiari, and Lorestan. In traditional medicine, this herb is considered as anti-pain, anti-neuralgia, antioxidant, antipyretic, and appetizer<sup>[62]</sup>. Sereshti *et al.*<sup>[63]</sup> investigated the effect of aqueous and alcoholic extracts of the plant *Stachys sylvatica* on *T. vaginalis* *in vitro*. Their results indicated that aqueous and alcoholic extracts of the plant after 72 hours in medium culture TYI-S-33 had no effect on *T. vaginalis*, and metronidazole was more effective than this extract<sup>[63]</sup>.

### ***Achillea millefolium*, *Juglans regia*, and *Artemisia absinthium***

*Achillea millefolium* is a flowering plant in the family Asteraceae. It is native to the temperate regions of the Northern Hemisphere in Asia, Europe, and North America. This plant has anti-inflammatory, antispasmodic and antioxidant activities<sup>[64]</sup>. *Juglans regia* belongs to the Juglandaceae family and *Juglans* genus and has tannin and naphthoquinones with potent bactericidal effects. The extract of this tree is used to treat headaches, colds, skin diseases, as well as fungal, bacterial and viral infections<sup>[65]</sup>. *Artemisia absinthium* belongs to the Asteraceae family and genus of *Artemisia*. This plant has medicinal properties, including insecticide and appetizer, as well as bactericidal, anti-inflammatory and antiparasitic effects<sup>[66]</sup>. The leaves extracts of *Achillea millefolium*, *Artemisia absinthium*, and *Juglans regia* on *T.*

*vaginalis* was studied by Khalili *et al.*<sup>[67]</sup> *in vitro*. All three plant extracts represented anti-trichomoniasis activity after 24 hour and parasites immobility increased. However, six hours after cultivation with *Achillea millefolium*, *Artemisia absinthium*, and *Juglans regia* extracts at the concentrations of 800, 400, and 800 mg/ml, respectively, all parasites were died<sup>[67]</sup>.

### ***Tanacetum parthenium***

*Tanacetum parthenium* (local name: fever few) belongs to *Asteraceae* family and is a native plant in Iran<sup>[68,69]</sup>. *Tanacetum parthenium*, as a traditional medicinal herb, is commonly used to prevent migraine headaches and has been used as a herbal treatment to reduce fever, arthritis, and digestive problems<sup>[68,69]</sup>. Its main compound is tannin, and others compounds include lactones (parthenolide and canine) and terpenes<sup>[68,69]</sup>. Study of the effect of hydro-alcoholic extract of *Tanacetum Parthenium* on *T. vaginalis* was conducted by Arefkhah *et al.*<sup>[69]</sup>. Alcoholic extract of this plant with concentrations of 4, 5, 8, and 10 mg/ml showed the same lethal effect on the parasite as compared to metronidazole, but concentrations of 1 and 1.25 indicated no effect<sup>[69]</sup>.

### ***Taxus baccata***

*Taxus baccata* is a conifer native to Western, Central and Southern Europe, as well as Northwestern Africa, Northern Iran, and Southwestern Asia<sup>[70,71]</sup>. This traditional medicine plant has antibacterial, antifungal, anti-inflammatory and antitumoral activities and is used for treating malaria, rheumatism, bronchitis, and asthma<sup>[70,71]</sup>. In 2013, Zarea *et al.*<sup>[71]</sup> investigated the effects of *Taxus baccata* leaves fractions on *T. vaginalis* growth in culture medium. The component of 60% of crude extract at concentrations of 200, 300, 400, and 500 µg/ml indicated higher anti-*T. vaginalis* effects than 90% ( $P < 0.05$ ). Concentration of 200 µg/ml of the extract of 60% caused 100% inhibition, but the component of 90% indicated 60% growth inhibition<sup>[71]</sup>.

### ***Viola odorata***

*Viola odorata* is a species of the genus *Viola* that is native to Europe and Asia and has been introduced to North America and Australia. In herbal medicine, *V. odorata* has been used for treating a variety of respiratory ailments, insomnia, and skin disorders<sup>[72,73]</sup>. Its compounds include phenolics, violin, and glycosides. In the leaves of this plant, analgesic components are salicylic acid glycosides<sup>[72,73]</sup>. The effects of different extracts of *Viola odorata* on *T. vaginalis* in culture medium has investigated by Salehi *et al.*<sup>[73]</sup>. The crude extract of leave (4 mg/ml), flower

(4 mg/ml), and root (2 mg/ml) of *Viola odorata* showed 100% growth inhibition after 24 hours<sup>[73]</sup>.

### ***Pelargonium roseum***

*Pelargonium roseum* belongs to the Geraniaceae family and *Pelargonium* genus. The major compounds of this plant are geranium, citronellol, mannitol, and ethyl alcohol<sup>[74,75]</sup>. It is used in traditional medicine as analgesic, anti-dysentery, and disinfectants as well as an anti-inflammatory, a hemostatic, and an antiseptic drug<sup>[74,75]</sup>. Fakhrie-Kashan *et al.*<sup>[75]</sup> studied the effects of aqueous and alcoholic extracts of *Pelargonium roseum* on the growth of *T. vaginalis in vitro*. IC50s (inhibitory concentration, 50%) of aqueous and alcoholic extracts of *Pelargonium roseum* on the growth of *T. vaginalis* after 24 h were 54.67 and 27.63 µg/ml, respectively<sup>[75]</sup>.

### ***Verbascum thapsus***

*Verbascum thapsus* is a member of scrophulariaceae family. This biennial plant grows in a wide range of areas and can be two meters or more in height<sup>[76,77]</sup>. *Verbascum thapsus* contains bioactive substances such as saponins, glycosides, glycosoaminoglycans, phenyl ethanol, and verbascose<sup>[76,77]</sup> and also chemical components that reduce cyclooxygenase activity. These components have anti-inflammatory activity and germicide and skin restore effects<sup>[76,77]</sup>. *Verbascum thapsus* has also been used to treat genital and urinary tract infections and diarrhea<sup>[76,77]</sup>. Induction of apoptosis in *T. vaginalis* due to the extract of this plant have been reported by Kashan *et al.*<sup>[77]</sup>. IC50s (inhibitory concentration, 50%) of ethanolic extract of *Verbascum thapsus* and metronidazole after 24 h were 39.17 and 0.0326 µg/ml, respectively. Results of this study indicated that the percentage of apoptosis after treatment of parasites with various concentrations of *Verbascum thapsus* extract (25, 50, 100, 200, and 400 µg/ml) were 20.7, 37.04, 47.5, 62.72, and 86.35 respectively<sup>[77]</sup>.

### ***Allium cepa, Oliveria decumbens Vent, and Muscari neglectum***

The onion is a vegetable and the most widely cultivated species of the genus *Allium*. This plant grows in most parts of the world and Iran flora. It is used in traditional medicine for treatment of diseases of kidney, bladder, and prostate<sup>[78]</sup>. *Oliveria decumbens Vent* belongs to Umbeliferae family and grows in Southern Iran. It is bactericide and contains tymol, threpenin, and carvacrol<sup>[79]</sup>. *Muscari neglectum* is native to the Mediterranean region<sup>[80,81]</sup>. In 2015, Fakhrieh-Kashan *et al.*<sup>[81]</sup> investigated the *in vitro* therapeutic effect of alcoholic extracts *Allium cepa*,

*Oliveria decumbens* Vent, and *Muscari neglectum* against *T. vaginalis*. In this study, IC50s of *Allium cepa*, *Oliveria decumbens* Vent, and *Muscari neglectum* ethanol extracts after 24 h were 572.3, 101.8, and 329.4 µg/ml, respectively<sup>[81]</sup>.

In conclusion, trichomoniasis is considered as one of the most common sexually transmitted diseases in humans<sup>[1,2]</sup>. Increasing resistance to drugs such as metronidazole leads to a serious problem; thus, new effective tactics are needed to treat this infection. The current medications and the first-line drugs for treatment of trichomoniasis are metronidazole and tinidazole; both are 5-nitroimidazole drugs approved by the US FDA. Besides, using metronidazole is limited because of its high toxicity, high doses, and development of drug resistance<sup>[30,37-39]</sup>. In order to improve the treatment of *T. vaginalis* infection, natural products could be a source of new drugs with low toxicity and high activity. Recently, many efforts have been made for the evaluation of the effects of plants on the pathogenic microorganisms that can lead to vaginal infection. Due to the diversity of Iranian medicinal plants, several studies have carried out on the *T. vaginalis* using these herbs. Unfortunately, previous studies have not used an identical procedure; therefore, we cannot exactly explain which plant extracts are more effective on the parasite. However, we can draw the conclusion that all plants with the largest effect on the parasites contain the following active compounds: cineol, tannins, flavonoid, terpenoid, phenolic ones, Artemisia, lactones, glycosides, geranium, citronium, mannitol, saponins, glycosoaminoglycans, verbascose, phenyl ethanol, tymol, threpenin, carvacrol, zingerone, paradol, gingerols, shogaols, inulin, polyacetylene, arctic aside. Until now, no herbal extract has been introduced as an approved drug for the treatment of trichomoniasis. More accurate and comprehensive studies are needed to achieve the desired results in the use of plants in trichomoniasis treatment.

**CONFLICT OF INTEREST.** None declared

## REFERENCES

- Harp DF, Chowdhury I. Trichomoniasis: evaluation to execution. *European journal of obstetrics and gynecology and reproductive biology* 2011; **157**(1): 3-9.
- Sutton M, Sternberg M, Koumans EH, McQuillan G, Berman S, Markowitz L. The prevalence of *Trichomonas vaginalis* infection among reproductive-age women in the United States, 2001-2004. *Clinical infectious diseases* 2007; **45**(10): 1319-1326.
- Tobin W. Alfred Donné and Léon Foucault: the first applications of electricity and photography to medical illustration. *Journal of visual communication in medicine* 2006; **29**(1): 6-13.
- Nijhawan AE, Chapin KC, Salloway R, Andrea S. Prevalence and predictors of trichomonas infection in newly incarcerated Women. *Sexually transmitted diseases* 2012; **39**(12): 973-978.
- Mao M, Liu HL. Genetic diversity of *Trichomonas vaginalis* clinical isolates from Henan province in central China. *Pathogens and global health* 2015; **109**(5): 242-246.
- Dirkx M, Boyer MP, Pradhan P, Brittingham A, Wilson WA. Expression and characterization of a β-fructofuranosidase from the parasitic protist *Trichomonas*. *BMC biochemistry* 2014; **15**: 12.
- World Health Organization, Dept. of Reproductive Health and Research. REterieved from: [http://www.who.int/reproductivehealth/about\\_us/en/](http://www.who.int/reproductivehealth/about_us/en/).
- Sharafi SM, Yousefi M, Yousefi HA, Asghari G, Darani HY. *In vitro* effects of various plants extracts on the growth of *Trichomonas vaginalis*. *Infectious disorders drug targets* 2013; **13**(5): 322-327.
- Sariego I, Monzote L, Rojas L. Setting a colorimetric assay with MTT for assessment of trichomonocidal activity. *Current clinical pharmacology* 2014; **9**(3): 283-287.
- Sutton M, Sternberg M, Koumans EH, McQuillan G, Berman S, Markowitz L. The prevalence of *Trichomonas vaginalis* infection among reproductive-age women in the United States, 2001-2004. *Clinical infectious diseases* 2007; **45**(10): 1319-1326.
- Sena AC, Miller WC, Hobbs MM, Schwebke JR, Leone PA, Swygard H, Atashili J, Cohen MS. *Trichomonas vaginalis* infection in male sexual partners: implications for diagnosis, treatment, and prevention. *Clinical infectious diseases* 2007; **44**(1): 13-22.
- Manshoori A, Mirzaei S, Valadkhani Z, Kazemi Arababadi M, Rezaeian M, Zainodini N, Bahramabadi R, Zare-Bidaki M. A diagnostic and symptomatological study on trichomoniasis in symptomatic pregnant women in Rafsanjan, South Central Iran in 2012-13. *Iranian journal of parasitology* 2015; **10**(3): 490-497.
- Secor WE, Meites E, Starr MC, Workowski KA. Neglected parasitic infections in the United States: trichomoniasis. *American journal of tropical medicine and hygiene* 2014; **90**(5): 800-804.
- Camila BM, Mariana dos SM, Tiana TASCA. Comparison of permanent staining methods for the laboratory diagnosis of trichomoniasis. *Revista do instituto de medicina tropical de são Paulo* 2016; **58**: 5.
- Mahmoud A, Sherif NA, Abdella R, El-Genedy AR, El Kateb AY, Askalani AN. Prevalence of *Trichomonas vaginalis* infection among Egyptian women using culture and Latex agglutination: cross-sectional study. *BMC womens health* 2015; **15**: 7.
- Khatoun R, Jahan N, Ahmad S, Khan HM, Rabbani T. Comparison of four diagnostic techniques for detection of *Trichomonas vaginalis* infection in females attending tertiary care hospital of North India. *Indian journal of pathology and microbiology* 2015; **58**(1): 36-39.
- Ali V, Nozaki T. Current therapeutics, their problems,

- and sulfur-containing-amino-acid metabolism as a novel target against infections by "amitochondriate" protozoan parasites. *Clinical microbiology reviews* 2007; **20**(1): 164-187.
18. Forbes GL, Drayton R, Forbes GD. A case of metronidazole-resistant *Trichomonas vaginalis* in pregnancy. *International journal of STD and AIDS* 2016; **27**(10): 906-908.
  19. Hawkins I, Carne C, Sonnex C, Carmichael A. Successful treatment of refractory *Trichomonas vaginalis* infection using intravenous metronidazole. *International journal of STD and AIDS* 2015; **26**(9): 676-678.
  20. Meites E, Gaydos CA, Hobbs MM, Kissinger P, Nyirjesy P, Schwebke JR, Secor WE, Sobel JD, Workowski KA. A review of evidence-based care of symptomatic trichomoniasis and asymptomatic *Trichomonas vaginalis* infections. *Clinical infectious diseases* 2015; **61**(8): 837-848.
  21. Kausar H, Qadir M, Anwar W. Ocular side effect of tinidazole: A rare case report. *Journal of family medicine and primary care* 2014; **3**(4): 467-469.
  22. Gretchen LJ. Tinidazole (Tindamax) for *Trichomonas* and bacterial vaginosis. *American family physician* 2009; **79**(2): 102-105.
  23. Thulkar J, Kriplani A, Agarwal N. A comparative study of oral single dose of metronidazole, tinidazole, secnidazole and ornidazole in bacterial vaginosis. *Indian journal of pharmacology* 2012; **44**(2): 243-245.
  24. McCann JS, Horner T, Shepherd I, Quin N. 2-day treatment of trichomoniasis with nimorazole. *The British journal of venereal diseases* 1974; **50**(5): 375-376.
  25. Fox LM, Saravolatz LD. Saravolatz. Nitazoxanide: a new thiazolide antiparasitic agent. *Clinical infectious diseases* 2005; **40**(8): 1173-1180.
  26. Dan M, Sobel JD. Failure of nitazoxanide to cure trichomoniasis in three women. *Sexually transmitted diseases* 2007; **34**(10): 813-814.
  27. Lushbaugh WB, Cleary JD, Finley RW. Cytotoxicity of hamycin for *Trichomonas vaginalis*, HeLa and BHK-21. *The journal of antimicrobial chemotherapy* 1995; **36**(5): 795-780.
  28. Tayal SC, Ochogwu SA, Bunce H. Paromomycin treatment of recalcitrant *Trichomonas vaginalis*. *International journal of STD and AIDS* 2010; **21**(3): 217-218.
  29. Cudmore SL, Delgaty KL, Hayward-McClelland SF, Petrin DP, Garber GE. Treatment of infections caused by metronidazole-resistant *Trichomonas vaginalis*: *clinical microbiology reviews* 2004; **17**(4): 783-793.
  30. Löfmark S, Edlund C, Nord CE. Metronidazole is still the drug of choice for treatment of anaerobic infections. *Clinical infectious diseases* 2010; **50**(Suppl1): S16-S23.
  31. Land KM, Johnson PJ. Molecular basis of metronidazole resistance in pathogenic bacteria and protozoa. *Drug Resistance Updates* 1999; **2**(5): 289-294.
  32. Vermani K, Garg S. Herbal medicines for sexually transmitted disease and AIDS. *Journal of ethnopharmacology* 2002; **80**(1): 49-66.
  33. Ezz Eldin HM, Badawy AF. *In vitro* anti-trichomonas *vaginalis* activity of Pistacia lentiscus mastic and Ocimum basilicum essential oil. *Journal of parasitic disease* 2015; **39**(3): 465-473.
  34. El-Sherbiny GM, El Sherbiny ET. The Effect of Commiphora molmol (Myrrh) in treatment of *Trichomoniasis vaginalis* infection. *Iranian Red Crescent medical journal* 2011; **13**(7): 480-486.
  35. Yan Y, Gao XZ. Protein analysis of *Trichomonas vaginalis* treated by *Pulsatilla chinensis* *in vitro*. *Zhongguo ji sheng chong xue yu ji sheng chong bing za zhi* 2010; **28**(3): 231-233.
  36. Ertabaklar H, Kivçak B, Mert T, Ozensoy Töz S. *In vitro* activity of *Arbutus unedo* leaf extracts against *Trichomonas vaginalis* trophozoites. *Turkiye parazitolojii dergisi* 2009; **33**(4): 263-265.
  37. Narcisi EM, Secor WE. *In vitro* effect of tinidazole and furazolidone on metronidazole-resistant *Trichomonas vaginalis*. *Antimicrobial agents and chemotherapy* 1996; **40**(5): 1121-1125.
  38. Sherrard J, Ison C, Moody J, Wainwright E, Wilson J, Sullivan A. United Kingdom national guideline on the management of *Trichomonas vaginalis* 2014. *International journal of STD and AIDS* 2014; **25**(8): 123-137.
  39. Sarma GR, Kamath V. Acute painful peripheral neuropathy due to metronidazole. *Neurology India* 2005; **53**(3): 372-273.
  40. Schwebke JR, Barrientes FJ. Prevalence of *Trichomonas vaginalis* isolates with resistance to metronidazole and tinidazole. *Antimicrobial agents chemotherapy* 2006; **50**(12): 4209-4210.
  41. Semnani MK, Saeidi M, Mahdavi MR, Rahimi F. Antimicrobial effects of methanolic extracts of some species of stachys and phlomis. *Journal of Mazandaran university of medical sciences*. 2007; **17**(57): 57-66.
  42. Forbes GL, Drayton R, Forbes GD. A case of metronidazole-resistant *Trichomonas vaginalis* in pregnancy. *International journal of STD and AIDS* 2015; **27**(10): 906-908.
  43. Hashemi P, Abolghasemi MM, Fakhari AR, Ebrahimi SN, Ahmadi S. Hydrodistillation-solvent micro-extraction and GC-MS identification of volatile components of *Artemisia aucheri*. *Chromatographia* 2007; **66**(3-4): 283-286.
  44. Zomorodian K, Saharkhiz MJ, Rahimi MJ, Bandegi A, Shekarkhar G, Bandegani A, Pakshir K, Bazargani A. Chemical composition and antimicrobial activity of the essential oil of *Zataria multiflora*. *Pharmacognosy magazine* 2006; **19**(2): 52-59.
  45. Saleem M, Nazli R, Afza N, Sami A, Ali MS. Biological significance of essential oil of *Zataria multiflora* Boiss. *Natural products research* 2004; **18**(6): 493-497.
  46. Abbasgholizadeh N, Ettehad GH, Arab R, Nemati A, Barak M, Pirzadeh A, Zarei M. Antibacterial effects of *Zataria multiflora* Boiss. (Shiraz oregano essence) on *Enterobacteriaceae* species. *Research journal of biological sciences* 2008; **3**(3): 345-347.
  47. Ettehad GH, Arab R. Evaluation of antibacterial effects of Shiraz oregano essence (*Zataria multiflora* Boiss) on

- Salmonella typhi* and comparing to antibiotics. *Research journal of biological sciences* 2007; **2**(6): 674-676.
48. Burt S. Essential oils: their antibacterial properties and potential applications in foods—a review. *International journal of food microbiology* 2004; **94**(3): 223-253.
  49. Chryssavgi G, Vassiliki P, Athanasios M, Kibouris T, Michael K. Essential oil composition of *Pistacia lentiscus* L. and *Myrtus communis* L.: evaluation of antioxidant capacity of methanolic extracts. *Food chemistry* 2008; **107**(3):1120-1130.
  50. Kalembe D, Kunicka A. Antibacterial and antifungal properties of essential oils. *Current medicinal chemistry* 2003; **10**(10): 213-229.
  51. Ziaie H, Azadbakht M, Abdollahi F, Shabankhani B. Effect of methanolic extracts of *Artemisia aucheri* Boiss., *Zataria multiflora* Boiss. and *Myrtus communis* L. on *Trichomonas vaginalis* (in vitro). *Journal of Gorgan university of medical sciences* 2006, **8**(1): 34-38.
  52. Benkeblia N. Antimicrobial activity of essential oil extracts of various onions (*Allium cepa*) and garlic (*Allium sativum*). *LWT-food science and technology* 2004; **37**(2): 263-268.
  53. Mikaili P, Maadirad S, Moloudizargari M, Aghajanshakeri S, Sarahroodi S. Therapeutic uses and pharmacological properties of Garlic, Shallot, and their biologically active compounds. *Iranian journal of basic medical sciences* 2013; **16**(10): 1031-1048.
  54. Lee CL, Chiang LC, Cheng LH, Liaw CC, Abd El-Razek MH, Chang FR, Wu YC. Influenza A (H1N1) antiviral and cytotoxic agents from *Ferula assafoetida*. *Journal of natural products* 2009; **72**(9): 1568-1572.
  55. Mahendra P, Bisht Sh. *Ferula asafoetida*: Traditional uses and pharmacological activity. *Pharmacognosy reviews* 2012; **6**(12): 141-146.
  56. Bahadoor Sarkari, Hadisa Tadayon, Shahrbanoo Askarian, Elahm Farnia, Mehrangiz Askarian. In vitro anti-Trichomonas activity of *Freula assafoetida* and garlic extract. *Journal of Gorgan university of medical sciences* 2009; **11**(3): 13-17.
  57. Danh LT, Han NL, Triet NDA, Zhao J, Mammucari R, Foster N. Comparison of chemical composition, antioxidant and antimicrobial activity of lavender (*Lavandula angustifolia* L.) essential oils extracted by supercritical CO<sub>2</sub>, hexane and hydrodistillation. *Food and bioprocess technology* 2012; **6**(12): 3481-3489.
  58. Jianu C, Pop G, T Gruia A, Horhat FG. Chemical composition and antimicrobial activity of essential oils of lavender (*Lavandula angustifolia*) and lavandin (*Lavandula x intermedia*) grown in Western Romania. *International journal of agriculture and biology* 2013; **15**(4): 772-776.
  59. Ezatpur B, Badparva E, Ahmadi Sh, Rashidipur M, Ziaie H. Investigation of anti *Trichomonas vaginalis* activity of *Lavandula angustifolia* essential oil in invitro media. *Journal of Ilam university of medical sciences* 2009; **16** (4): 31-38.
  60. Huang HC, Ho YC, Lim JM, Chang TY, Ho CL, Chang TM. Investigation of the anti-melanogenic and antioxidant characteristics of Eucalyptus camaldulensis flower essential oil and determination of its chemical composition. *International journal of molecular sciences* 2015; **16**(5): 10470-10490.
  61. Hassani S, Asghari Gh, Yousefi H, Kazemian A, Rafieiean M, Yousofi Darani H. Effects of different extracts of Eucalyptus camaldulensis on *Trichomonas vaginalis* parasite in culture medium. *Advanced biomedical research* 2013; **2**: 47.
  62. Hajdari A, Novak J, Mustafa B, Franz C. Essential oil composition and antioxidant activity of *Stachys sylvatica* L. (Lamiaceae) from different wild populations in Kosovo. *Natural product research* 2012; **26**(18): 1676-1681.
  63. Sereshti M, Yousofi Darani H, Zebardast N, Rafean M, Manochehre Naeni K, Yousofi HA. Effect of ethanolic and watery extract of aerial parts of *Stachys Lavandulifolia* on *Trichomonas vaginalis*, in vitro. *Journal of medicinal plants* 2012; **1**(41): 159-165.
  64. Kotan R, Cakir A, Dadasoglu F, Aydin T, Cakmakci R, Ozer H, Kordali S, Mete E, Dikbas N. Antibacterial activities of essential oils and extracts of Turkish *Achillea*, *Satureja* and *Thymus* species against plant pathogenic bacteria. *Journal of the science of food and agriculture* 2010; **190**(1): 145-160.
  65. Yang H, Sung SH, Kim YC. The ethanolic extract of *Juglans sinensis* leaves and twigs attenuates CCl<sub>4</sub>-induced hepatic oxidative stress in rats. *Pharmacognosy magazine* 2015; **11**(43): 533-539.
  66. Jasna MC, Sonja MD, Gordana SC, Vesna TT. Free-radical scavenging activity of wormwood (*Artemisia absinthium*) extracts. *Journal of the science of food and agriculture* 2004; **85**(2): 265-272.
  67. Khalili B, Rafieian M, Hejazi SH, Yusefi HA, Yektaian N, Shirani-Bidabadi L. Effect of *Achillea millefolium*, *Artemisia absinthium* and *Juglans regia* leaves extracts on *Trichomonas vaginalis*, in vitro. *Journal of Shahrekord university of medical sciences* 2011; **12**(4): 62-69.
  68. Rabito MF, Britta EA, Pelegrini BL, Scariot DB, Almeida MB, Nixdorf SL, Nakamura CV, Ferreira IC. In vitro and in vivo antileishmania activity of sesquiterpene lactone-rich dichloromethane fraction obtained from *Tanacetum parthenium* (L.) Schultz-Bip. *Experimental parasitology* 2014; **143**: 18-23.
  69. Arefkhah N, Taghipur S, Yousefi M, Rafeiean M, Daneshpur S, Yousefi H. In-vitro effect of hydro-alcoholic extract of tanacetum parthenium extract on *Trichomonas vaginalis*. *Journal of Isfahan medical school* 2013; **31**(236): 623-629.
  70. Bernhoft A. Bioactive Compounds in Plants—Benefits and Risks for Man and Animals. Oslo: The Norwegian Academy of Science and Letters, 2010.
  71. Zarea A, Asghari GHR, Ghanadian M, Yousefi HA, Yousofi Darani H. Effect of *Taxus baccata* leaves fractions on *Trichomonas vaginalis* growth in culture medium. *Armaghane danesh* 2014; **18**(11): 888-899.
  72. Siddiqi HS, Mehmood MH, Rehman NU, Gilani AH. Studies on the antihypertensive and antidyslipidemic activities of *Viola odorata* leaves extract. *Lipids in health and disease* 2012; **11**: 6.



73. Salehi L, Asghari Gh, Yousofi H, Yousofi Darani H. Effects of different extracts of *Viola odorata* on *Trichomonas vaginalis* in culture medium. *Journal of Isfahan medical school* 2014; **31**(266): 2139-2148.
74. Edris AE. Pharmaceutical and therapeutic potentials of essential oils and their individual volatile constituents: a review. *Phytotherapy research* 2007; **21**(4): 308-323.
75. Fakhrie-Kashan Z, Arbabi M, Delavari M, Taghi-Zadeh M, Hooshyar H, Solaymani F. The effect of aqueous and alcoholic extracts of *Pelarqonium roseum* on the growth of *Trichomonas vaginalis* *in vitro*. *Feyz* 2014; **18**(4): 369-375.
76. Riaz M, Zia-Ul-Haq M, Jaafar, HZE Jaafar. Common mullein, pharmacological and chemical aspects. *Revista brasileira de farmacognosia* 2013; **23**(6): 948-959.
77. Kashan ZF, Arbabi M, Delavari M, Hooshyar H, Taghizadeh M, Joneydy Z. Effect of *Verbascum thapsus* ethanol extract on induction of apoptosis in *Trichomonas vaginalis* *in vitro*. *Infectious disorders- drug targets* 2015; **15**(2): 125-130.
78. Mantawy MM, Ali HF, Rizk MZ. Therapeutic effects of *Allium sativum* and *Allium cepa* in *Schistosoma mansoni* experimental infection. *Revista do instituto de medicina tropical de são paulo* 2011; **53**(3): 155-163.
79. Motamedi H, Darabpour E, Gholipour M, Nezhad SM. Antibacterial effect of ethanolic and methanolic extracts of *Plantago ovate* and *Oliveria decumbens* endemic in Iran against some pathogenic bacteria. *International journal of pharmacology* 2010; **6**(2): 117-122.
80. Nasrabadi M, Halimi M, Nadaf M. Phytochemical screening and chemical composition of extract of *Muscari neglectum*. *Middle-East journal of scientific research* 2013; **14**(4): 566-569.
81. Fakhrieh-Kashan Z, Arbabi M, Delavari M, Hooshyar H, Taghizadeh M. therapeutic effect of *Allium cepa*, *Oliveria decumbens* Vent and *Muscari neglectum* against *Trichomonas vaginalis*, *In vitro*. *Journal of research in medical sciences* 2015; **32**(310): 1985-1992.