

# The Antiviral Potential of Iranian Herbal Pharmacopoeia (IHP) on Herpes Simplex Viruses (HSV): A Review Article

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## Abstract

Herpes Simplex Viruses (HSV) viruses are highly contagious that commonly cause dermatitis, encephalitis, meningitis and genitourinary infections and also can lead to cervical cancer. For treatment of HSV infections, several physical methods and antiviral drugs are introduced, antiviral medications can also prevent or reduce outbreaks. The use of herbal medicine with antiviral effects attracted worldwide attentions. The aim of this review article is to introduce the Iranian Herbal Pharmacopoeia (IHP) with antiviral potential against two HSV serotypes and help to evaluate and develop the new drugs from natural sources. To provide this review, relevant articles in some authentic databases including PubMed, Web of Science, Science Direct, Scopus, Google Scholar and SID (scientific information database), from 1967 to April 2022 were collected, and selected botanicals from (IHP) with their scientific names and classifications and their outcome (CC<sub>50</sub> and IC<sub>50</sub>) were introduced. In this review, scientific data regarding anti-herpetic activities of Iranian Herbal Pharmacopoeia (IHP) showed that 34 herbs from 17 families have antiviral potential to inhibit two HSV serotypes. According to families, Lamiaceae family has the highest percentage (29.41 %) of plants with antiviral activity against two HSV serotypes, also review of recent data showed that *Salvia officinalis*, *Melissa officinalis*, *Securigera Securidaca*, *Hyssopus officinalis*, *Quercus brantii*, *Artemisia aucheri* and *Curcuma longa* have remarkable antiviral activity against two HSV serotypes. Results of this review suggest that further research to identify and purify the bioactive compounds to determine the molecular mechanisms of action is needed.

**Keywords:** herpes simplex; herbal medicine; pharmacopoeia; antiviral; drugs.

## INTRODUCTION

Herpes simplex virus (HSV) belongs to the Herpesviridae family and Alphaherpesvirinae subfamily (Álvarez et al. 2020), is a global public health issue that can cause serious infection and classified into 2 serotypes: HSV-1 and HSV-2 (Gavanji et al. 2015; Pebody et al. 2004). The HSV genome consists of linear double-strand DNA, that causes primary and recurrent lesions (Reuven et al. 2003) HSV viruses are highly contagious that commonly cause dermatitis, encephalitis, meningitis and genitourinary infections and also can lead to cervical cancer (Kłysik et al. 2020; Elad et al. 2010). HSV-1 or oral herpes mainly occurs on the face, chin, lips and mouth area which infection with this serotype causes small blisters or cold sores and inflammation of oral and eye cells (Asai and Nakashima 2018; Vaghela et al. 2021), ranging from mild to severe, that may develop and increase the risk of serious illness (Farooq and Shukla 2012; Anderson et al. 2014). This type of virus usually transmitted via oral secretions or direct contact with cold sores and it can cause more severe complications such as conjunctivitis (Koujah et al. 2019), herpetic stromal keratitis (HSK) (Stuart and

Keadle 2012), gingivostomatitis (George and Anil 2014) and HSV-1 encephalitis (HSE) (Feola et al. 2018). HSV-2, infection is usually transmitted through sexual contacts (Zhang et al. 2022) and affects the genital area and increased risk of human immunodeficiency virus (HIV) transmission (Crisci et al. 2019). For treatment of HSV infections, several physical methods and antiviral drugs such as valacyclovir, acyclovir, penciclovir, cidofovir, and famciclovir are introduced (Sadowski et al. 2021). The antiherpetic agents target and inactivate viral DNA polymerase enzyme and inhibit the proliferation and viral replication (Li et al. 2019). Acyclovir (ACV) is an antiviral agent which widely used to control and treatment of HSV infections (Wei et al. 2021). In the process of drug action, the ACV converts to acyclovir triphosphate (acyclo-GTP) and inhibits viral DNA polymerase (Fyfe et al. 1978). Nowadays, due to the resistance mutations and tolerant enzyme production, especially in people with immunodeficiency disorders, urgent need to investigate the new antiviral drugs has been highlighted (Roy et al. 2022; Majewska and Młynarczyk-Bonikowska 2022; Chuerduangphui et al. 2022). Numerous research studies have been done to investigate the novel antiviral agents

(Jassim and Naji 2003), and many anti-herpetic drugs have been approved (Sadowski et al. 2021), also researchers have been contributing to develop and produce a new vaccine against herpes infection but, no preventive HSV vaccines have been approved (Krishnan and Stuart 2021). The use of herbal medicine with antiviral effects attracted worldwide attentions (Gavanji et al. 2014). Scientific research has shown that natural bioactive compounds like flavonoids, terpenes, phenols and alkaloids have anti-HSV properties (Pesola and Coen 2008; Tolo 2006). Among the compounds mentioned, phenolic classes are the most commonly used for their anti-HSV properties (Tremel et al. 2020) (Table 1). This article is a review which provides various information about the potential antiviral activity of Iranian Herbal Pharmacopoeia (IHP) on Herpes Simplex Viruses (HSV), and help to evaluate and develop the new drugs from natural sources.

## METHODS

To provide this review, all reported herbal medicine with antiviral effects against Herpes Simplex Viruses (HSV) were collected through Iranian Herbal Pharmacopoeia (IHP) (Ghasemi Dehkordi et al. 2003) and the most relevant articles in some authentic databases including PubMed, Web of Science, Science Direct, Scopus, Google Scholar and SID (scientific information database), from 1967 to April 2022 were searched. The search with different combinations of keywords were herbal medicine, herpes simplex viruses, antiviral agents, simplex virus, plants, Iran, herb. In this review, the selected articles and books were used to sets of the general and specific criteria to examine and present the medicinal plants with antiviral activities. Selected botanicals with their scientific names and classifications and their outcome ( $CC_{50}$  and  $IC_{50}$ ) are presented in the article.

## Antiviral activity of phytochemicals Against HSVs

Today, various compounds with antiviral activity are contributing in the most of the medicinal process for the cure of human viral infections (Singh et al. 2021; Mukhtar et al. 2008). Many studies have shown that naturally produced compounds with antiviral activity against two serotypes of HSV are polysaccharides (Jin et al. 2015), flavonoids (Flores et al. 2016), terpenes (Soares et al. 2007), Steroids (da Rosa Guimarães et al. 2013), saponins (Ogawa et al. 2021), tannins (Lin et al. 2011), Phenolic (Hassan et al. 2011), alkaloids (Chen et al. 2015), lignans (Chen et al. 2015), Miscellaneous (Tremel et al. 2020), proanthocyanidin (Terlizzi et al. 2016), quinones (Caruso et al. 2020) and thiosulfates (Rouf et al. 2020). Several antiviral mechanisms of these phytochemicals have been identified, which most of them were verified against RNA and DNA viruses (Jang et al. 2021; Zrig 2022), such as herpes simplex virus type 1 and type 2 (DNA viruses) (Liu et al. 2019). These compounds inhibit the specific processes in the viral replication cycle (Hassan et al. 2018), and viral entry to the target cells (Rouf et al. 2020), also they inhibit the viral gene and protein expression and suppress the NF- $\kappa$ B Activity (Hutterer et al. 2017) that can help to prevent the spread of viruses. Several studies have shown the antiviral mechanisms of these natural compounds against two HSV serotypes which are summarized in Table 1.

## Antiviral potential of Iranian Herbal Pharmacopoeia (IHP)

The present review focuses on selected Iranian Herbal Pharmacopoeia (IHP) with antiviral potential against two HSV serotypes. In this review, the articles were read and 34 herbs from 17 families were selected based on anti-herpetic activity and percentages of each families were calculated. According to families in IHP, Lamiaceae has the highest percentage (29.41 %) of plants with antiviral activity against two serotypes of HSV (Figure 1).

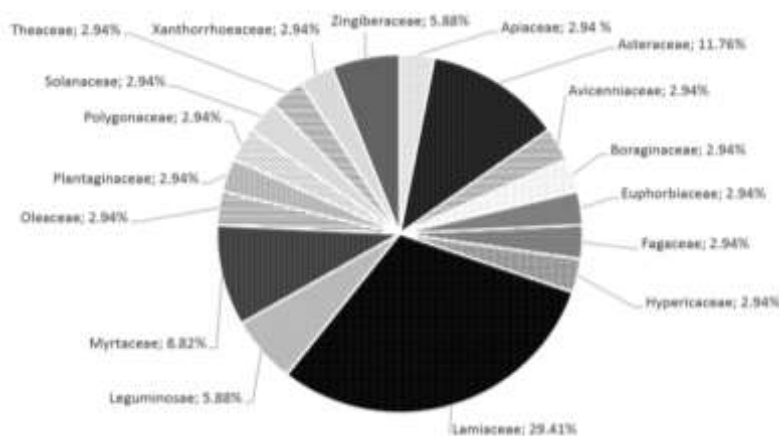


Figure 1. The percentages of plant families against two serotypes of HSV.

**Table 1.** Anti-herpetic activity of natural compounds.

No	Chemical groups	Compositions	Mechanisms	Serotype	References
1	Flavonoid	Curcumin	Affecting the viral transactivator protein VP16 -mediated recruitment of RNA polymerase II (Pol II) to Immediate early (IE) gene promoters and Inhibits the HSV-1 replication, Inhibition of HSV-1 and HSV-2 replication and adsorption	HSV-1/HSV-2	(Kutluay et al. 2008; Zalilawati et al. 2015; Zandi et al. 2010; Flores et al. 2016)
2	Flavonoid	Galangin	Inhibition of viral adsorption	HSV-1/HSV-2	(Lyu et al. 2005)
3	Flavonoid	Quercetin	Inhibiting expression of Glycoprotein D ( <i>gD</i> ) and Infected cell protein 0 (ICP0), and suppresses the <i>TLR-3</i>	HSV-1	(Lee et al 2017)
4	Flavonoid	Houttuynoid	Blocking membrane fusion	HSV-1	(Li et al 2017)
5	Flavonoid	Epicatechin gallate	Inhibition of viral adsorption, binding to HSV glycoproteins	HSV-1	(de Oliveira et al. 2013; Isaacs et al. 2008; Subramanian and Geraghty 2007)
6	Flavonoid	Isoquercitrin	Inhibition of NF-κB activation		(Hung et al. 2015)
7	Alkaloid	Harmine	Inhibition of viral replication and gene expression, reduction the NF-κB activation, and IκB-α degradation	HSV-1/HSV-2	(Hutterer et al. 2017; Chen et al 2015)
8	Phenolic	Psoromic acid	Inhibition of HSV-1 DNA polymerase	HSV-1	(Hassan et al. 2011)
9	Phenolic	Protocatechuyl aldehyde	Inhibition of viral replication	HSV-1	(Li et al 2005; Hao 2019)
10	Phenolic	Kuwanon X	Inhibition of HSV-1 adsorption and reduction of (IE) gene expression and viral DNA synthesis	HSV-1	(Ma et al. 2016)
11	Tannins	Chebulagic acid (CHLA)	Blocking the interactions of virus and target cells	HSV-1	(Lin et al. 2011)
12	Tannins	Punicalagin (PUG)	Blocking the interactions of virus and target cells	HSV-1	(Lin et al. 2011)
13	Tannins	Chebulinic acid (	Inhibition of viral attachment to the target cells	HSV-2	(Kesharwani et al. 2017)
14	Tannins	Samarangenin	Inhibition of viral replication	HSV-1	(Kuo et al. 2002)
15	Diterpenes	Epitaondiol	Maybe target the HSV-1 replication	HSV-1	(Soares et al. 2007)
16	Miscellaneous	(E)-2-(2,4-hexadiynyliden) - 1,6-dioxaspiro[4.5]dec-3-ene	inhibition of viral gene expression	HSV-1	(Álvarez et al. 2015)
17	Polysaccharide	Eucheuma gelatinae polysaccharide (EGP)	Blocking the viral entry to the target cells by inactivating the viral particles, Inhibition of viral intracellular biosynthesis	HSV-1	(Jin et al. 2015)
18	Polysaccharide	Sulfated polysaccharide	Inhibition of HSV-1 replication and viral entry to the target cells	HSV-1	(Zhu et al. 2006)
19	Polysaccharide	Polysaccharide Boergeseniella thuyoides	Inhibition of virus adsorption	HSV-1	(Bouhlal et al. 2011)
20	Polysaccharide	Alginic acids and Sulfated	Inhibition of viral attachment to the target cells by interaction with virus particles	HSV-1	(Saha et al. 2012)
21	Polyphenol	Mangiferin	Inhibition of viral replication	HSV-1	(Zheng and Lu 1990)
22	Polyphenol	Rosmarinic acid	Inhibition of viral replication and viral attachment to the target cells	HSV-1/HSV-2	(Astani et al 2014; Chen et al 2017)
23	Polyphenol	Yatein	Inhibiting expression of Infected-cell polypeptide 4 (ICP4) and Infected cell protein 0 (ICP0), and viral DNA synthesis	HSV-1	(Kuo et al 2006)
24	Monoterpenoid	Geraniol	Inhibition of viral replication	HSV-2	(Hassan et al. 2018)
25	Diterpenoid	Andrographolide	Inhibiting expression of Glycoprotein D	HSV-1	(Wiar et al. 2005)
26	Steroids	Halistanol sulfate	Inhibition of viral attachment to the target cells	HSV-1	(da Rosa Guimarães et al. 2013)
27	Organosulfur	Allicin	Inhibition of viral entry to the target cells		(Rouf et al 2020)
28	Triterpenoid	Glycyrrhizic acid methyl ester	Inhibition of viral replication	HSV-1	(Ikeda et al. 2005)
29	Triterpenoid	Ursolic acid	Inhibition of viral replication <sup>[78,79]</sup>	HSV-1/HSV-2	(Tshilanda et al. 2020; Bag et al. 2012)

### Apiaceae

Apiaceae family which is called Umbelliferae, includes a large number of medicinal plants with various therapeutic properties has a significant role in pharmaceutical development (Amiri and Joharchi 2016; Ekiert 2000). *Cuminum cyminum* belonging to family Apiaceae is an aromatic plant that can be used as medicinal herbs to treat various diseases (Sowbhagya 2013; Mnif and Aifa 2015; Gavanji et al. 2015) and flavoring agents to improve the flavor of foods (Johri 2011). Researchers have reported that methanol extract of *C. cyminum* showed the antiviral effects against HSV-1 (Table 2). Based on this study, the  $CC_{50}$ ,  $IC_{50}$  values were 0.45 and 0.18 mg/mL, respectively (Motamedifar et al. 2010). The molecular mechanism of *C. cyminum* against Herpes Simplex Virus has not yet been characterized, but the polyphenolic compounds in the extract may inhibit the HSV virus (Ani et al. 2006).

### Asteraceae

The Asteraceae family, or sunflower family, including several thousand plants, has a long history of use in traditional herbal medicine (THM), for the treatment of diseases (Amiri and Joharchi 2016; Ekiert 2000). *Artemisia aucheri* belonging to family Asteraceae is an aromatic and endemic plant in Iran, which is widely used for treatment of various diseases (Gavanji et al. 2014). This plant has been reported for its antiviral activities (Kshirsagar and Rao 2021), and Karamoddini et al assessed the antiviral properties of *Artemisia* species against HSV-1 which *Artemisia annua* inhibited this serotype at different concentrations (Karamoddini et al. 2011). Another study indicated that Aqueous extract of *A. aucheri* had Anti-herpetic property on HSV-1 and reduced the expression of UL46 and US6 genes, and the  $IC_{50}$  of this extract, 24.7  $\mu$ g/ml was determined (Zamanian et al. 2021). In the other study the anti-herpetic activity of aqueous extract of *A. aucheri* against HSV-1 was evaluated that viral infection significantly reduced at 50 and 75  $\mu$ g/ml (Zamanian et al. 2021). Research in 2015 showed that phenolic compounds in *Artemisia* has antiherpetic activity which can cause some abnormalities in the function and structure of herpes simplex virus (Gavanji et al. 2015). *Arctium lappa* is another member of Asteraceae family which possesses various therapeutic potential to treat infectious diseases (Bai et al. 2016), In addition *A. lappa* exhibited, anti-inflammatory (Pirvu et al. 2017), anticancer

(Leonard et al. 2006) and antiviral effects against two serotypes of HSV (Chan et al. 201; Dias et al. 2017). A study has been reported, that 400 mg/ml of hydroalcoholic extract of *A. lappa* inhibited the HSV-1 in in vitro condition (Dias et al. 2017) (Table 2).

*Echinacea purpurea* a species of Asteraceae family is widely used for the treatment of diseases (Shemluck 1982), such as chest & lung conditions, colds, coughs, candidiasis and influenza (Hudson et al. 2005). Furthermore, *E. purpurea* exhibited significant antiviral activity against HSV-1 (Thompson 1998). Also, Garcia et al. assessed the antiherpetic activity of *E. purpurea* against HSV-1 which the  $IC_{50}$  and  $CC_{50}$  values, were determined to be 500 and 900  $\mu$ g/ml, respectively (Farahani 2013). According to a study, chicoric acid exhibited antiviral properties against HSV-1 (Binns et al. 2002). Another in vivo study showed that *E. purpurea* polysaccharide (EP), antiviral effects on the development of HSV by promoting the immune response (Ghaemi et al. 2009). Another important species of Asteraceae family is *Tanacetum parthenium* which has been traditionally used to treat various diseases (Ghaemi et al. 2009). Benassi-Zanqueta et al. assessed the antiviral efficacy of chlorogenic acids and parthenolide which derived from *T. parthenium* against HSV-1 that results showed that chlorogenic acids was effective against HSV-1 (Benassi-Zanqueta et al. 2019). Base on this research, the hydroethanolic extract inhibited viral replication and the  $EC_{50}$  value was 18.1 mg/ml.

### Avicenniaceae

*Avicenna marina* is a member of Avicenniaceae family, which traditionally used for treatment of small pox, rheumatism and respiratory problems (Afzal et al. 2011; Namazi et al 2013). And has strong antiviral activity against HSV-1 (Chiang et al. 2003; Namazi et al, 2013; Behbahani et al. 2013). A study showed that glycerin extract of *A. marina*, inhibited the HSV-1 and the  $IC_{50}$  values before and after virus attachment and  $CC_{50}$  were determined to be 87.1, 41.9 and 5750.96  $\mu$ g/ml, respectively (Zandi et al. 2009). Based on the previous studies, *A. marina*, contains many phytochemicals with antiviral potentials to inhibit herpes simplex viruses (HSV). Several studies have shown that flavonoids in the *A. marina* extract plays a crucial role in antiviral activities against HSV-1 (Chiang et al. 2003; Namazi et al, 2013; Behbahani et al. 2013). (Table 2).

**Table 2.** Antiviral mechanism of Iranian Herbal Pharmacopoeia (IHP) against herpes simplex viruses (HSV-1 and -2)

No	Plant name	Family	Type of study (in vitro or in vivo)	Type of virus	Compounds and Mechanisms	References
1	<i>Aloe vera</i>	Xanthorrhoeaceae	In vitro	HSV-1/ HSV-2	Aloe-emodin inhibits the replication of viral enveloped	(Lin et al. 2008; Zandi et al. 2007; Rezazadeh et al. 2016)
2	<i>Artemisia aucheri</i>	Asteraceae	In vitro	HSV-1	Artemisinin inhibits the central regulatory processes and blocks the metabolic requirements of replication, reduces the UL46 and US6 genes	(Kshirsagar and Rao 2021; Karamoddini et al. 2011; Zamanian et al. 2021a; Zamanian et al. 2021b).
3	<i>Arctium lappa</i>	Asteraceae	In vitro	HSV-1	Arctigenin inhibits the viral replication, Phenolic constituents such as caffeic acid and chlorogenic acid inhibit the viral multiplication	(Dias et al. 2017; Wang et al. 2019; Yang et al 2005; Lal et al 2020; Chiang et al. 2002; Chan et al. 2011)
4	<i>Avicenna marina</i>	Avicenniaceae	In vitro	HSV-1	Luteolin inhibits the viral replication	(Chiang et al. 2003; Namazi et al. 2013)
5	<i>Camellia sinensis</i>	Theaceae	In vitro	HSV-1	Epicatechin gallate Inhibits the viral adsorption, binding to HSV glycoproteins	(de Oliveira et al. 2013; Isaacs et al. 2008; Subramanian and Geraghty 2007)
6	<i>Cuminum cyminum</i>	Apiaceae.	In vitro	HSV-1	EHP [1-(2-Ethyl, 6-Heptyl) Phenol] effects on the percentage of plaque	(Mohamadein et al. 2015; Motamedifar et al. 2010)
7	<i>Curcuma longa</i>	Zingiberaceae	In vitro	HSV-1/ HSV-2	Affecting the viral transactivator protein VP16 -mediated recruitment of RNA polymerase II (Pol II) to Immediate early (IE) gene promoters and Inhibits the HSV-1 replication, Inhibition of HSV-1 and HSV-2 replication and adsorption	(Hutterer et al. 2017; Kutluay et al. 2008; Zalilawati et al. 2015; Flores et al. 2016)
8	<i>Echium amoenum</i>	Boraginaceae	In vitro	HSV-1	Rosmarinic acid inhibits the viral attachment to host cells	(Flores et al. 2016; Chen et al. 2017)
9	<i>Echinacea purpurea</i>	Asteraceae	In vitro/In vivo	HSV-1	Cichoric acid interact and inhibit the virus activities	(Binns et al. 2002; Pluymers et al. 2000; Burlou-Nagy et al. 2022; Zhang et al. 2014)
10	<i>Euphorbia spinidens</i>	Euphorbiaceae	In vitro	HSV-1	Betulin and (3 $\beta$ ,23E)-cycloarta-23-ene-3,25-diol, the extract Inhibits the viral replication and adsorption	(Shamsabadipour et al. 2013; Karimi et al. 2016)
11	<i>Eucalyptus caesia</i>	Myrtaceae	In vitro	HSV-1	Unknown	(Schnitzler et al. 2001; Brezani et al. 2018; Mieres-Castro et al. 2021)
12	<i>Eucalyptus globulus</i>	Myrtaceae	In vitro	HSV-1	Grandinol, sideroxylin, and tereticornate inhibit the viral replication	(Schnitzler et al. 2001; Brezani et al. 2018; Mieres-Castro et al. 2021; Ma and Yao 2020; Mohan et al. 2020)
13	<i>Glycyrrhiza glabra</i>	Leguminosae	In vitro	HSV-1	glycyrrhizic acid (glycyrrhizin) inhibits the viral replication, suppress the growth	(Ghannad et al. 2014; Fukuchi et al. 2016; van Rossum et al. 1998; Cohen 2005; Huan et al. 2021)
14	<i>Hypericum perforatum</i>	Hypericaceae	In vitro/In vivo	HSV-1/ HSV-2	Hypericin Inhibits the viral adsorption	(Huan et al. 2021; Weber et al. 1994; Mohamed et al. 2022; Fritz et al. 2007; Westh et al. 2004; Béjaoui et al. 2017)
15	<i>Hyssopus officinalis</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Unknown	(Akram et al. 2018; Behbahani 2009; Schnitzler et al. 2019)
16	<i>Melissa officinalis</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Rosmarinic acid inhibits the viral attachment to host cells	(Astani et al 2014a; Astani et al. 2012b; Mazzanti et al. 2008)
17	<i>Mentha piperita</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Piperitenone oxide (PEO) and Menthol Inhibit the viral replication and adsorption	(Wolbling et al. 1994; Koytchev et al. 1999; Civitelli et al. 2014; Herrmann et al. 1967)
18	<i>Myrtus communis</i>	Myrtaceae	In vitro	HSV-1	Unknown	(Moradi et al. 2011; Alipour et al. 2014; Isaacs et al. 2008)

No	Plant name	Family	Type of study (in vitro or in vivo)	Type of virus	Compounds and Mechanisms	References
19	<i>Olea europaea</i>	Oleaceae	In vitro	HSV-1	Phenolic compounds such as caffeic acid inhibits the viral multiplication	(Motamedifar et al. 2015; Ben-Amor et al. 2021; Ikeda et al. 2011)
20	<i>Ocimum basilicum</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Ursolic acid and Apigenin Inhibit the viral replication	(Chiang et al. 2005; Bag et al. 2012; Lin et al. 2008)
21	<i>Plantago major</i>	Plantaginaceae	In vitro	HSV-1/ HSV-2	Caffeic acid inhibits the viral multiplication	(Chiang et al. 2002; Ben-Amor et al. 2021; Ikeda et al. 2011)
22	<i>Quercus Persica</i>	Fagaceae	In vitro	HSV-1	Tannic acid inhibits viral replication	(Chiang et al. 2005; Wu et al. 2022; Karimi et al. 2013; Kaczmarek 2020; Nance and Shearer 2013)
23	<i>Ricinus communis</i>	Euphorbiaceae	In vitro	HSV-1	The alkaloid and phenolic compound have antiherpetic activity	(Elkousy et al. 2021; Abdul et al. 1996)
24	<i>Rheum palmatum</i>	Polygonaceae	In vitro/In vivo	HSV-1	Unknown	(Abdul et al. 1996; Kurokawa et al. 1993; Chang et al. 2014; Shen et al. 2019)
25	<i>Rosmarinus officinalis</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Rosmarinic acid Inhibit of viral replication and viral attachment to the target cells	(Al-Megrin et al. 2020; Mancini et al. 2009; Hitl et al. 2021; Chen et al. 2017; Astani et al 2014)
26	<i>Salvia officinalis</i>	Lamiaceae	In vitro/In vivo	HSV-1/ HSV-2	Thujone, $\beta$ -caryophyllene linalyl acetate, alpha terpinyl acetate, and germacrene D have anti-herpetic activity	(Shen et al. 2019; Al-Megrin et al. 2020; Mancini et al. 2009; Hitl et al. 2009; Schnitzler et al. 2008; Rajbhandari et al. 2001; Santoyo et al. 2014; Ezema et al. 2022)
27	<i>Satureja hotensis</i>	Lamiaceae	In vitro	HSV-1	Unknown	(Hamidpour et al. 2014; Khalil et al. 2020)
28	<i>Securigera Securidaca</i>	Leguminosae	In vitro	HSV-1	Kaempferol and kaempferol-7-O-glucoside inhibit the HSV infection but the mechanism is unknown	(Behbahani et al. 2014; Behbahani et al. 2013)
29	<i>Solanum paniculatum</i>	Solanaceae	In vitro	HSV-1	Unknown	(Valadares et al. 2009; Kaunda and Zhang 2019)
30	<i>Tanacetum parthenium</i>	Asteraceae	In vitro/In vivo	HSV-1	Parthenolide did not directly act against HSV, and it can able to handle the defense mechanisms in host cells against viral particles	(Benassi-Zanqueta et al. 2019; Benassi-Zanqueta et al. 2018)
31	<i>Thymus vulgaris</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Thymol reduces the viral transmission	(Gavanji et al. 2015; Catella et al. 2021; Nolkemper et al. 2006; Sharifi-Rad et al. 2017; Lai et al. 2012)
32	<i>Thymus kotschyanus</i>	Lamiaceae	In vitro	HSV-1/ HSV-2	Borneol, and isoborneol that inhibits the viral replication	(Farahani 2017; Yang et al. 2020)
33	<i>Zataria multiflora</i>	Lamiaceae	In vitro	HSV-1	Rosmarinic acid inhibits the viral attachment to host cells	(Arabzadeh et al. 2020; Ben-Shabat et al. 2020; Mardani et al. 2012; Astani et al 2014; Chen et al 2017)
34	<i>Zingiber officinale</i>	Zingiberaceae	In vitro/In vivo	HSV-1	Unknown	(Schnitzler et al. 2012; Camero et al. 2019; Koch et al. 2008; Hayati et al. 2021)

### Boraginaceae

*Echium amoenum*, commonly known as borage, belongs to the family Boraginaceae (Zannou et al. 2021), which has a long history in Iranian traditional medicine (ITM) for treatment of influenza and infectious diseases (Ranjbar et al. 2006). This plant has antiviral properties against HSV-1, and the IC<sub>50</sub> and CC<sub>50</sub> values were determined to be 500 and 1000 µg/ml, respectively, also the results of this research showed that virus replication was inhibited at the lower concentration than 400 µg/ml (Abolhassani 2010; Farahani 2013).

### Euphorbiaceae

*Euphorbia spinidens*, a member of Euphorbiaceae family, is traditionally used as antiasthmatic, relieving stomachache, laxative and emetic (Ghanadian et al. 2016). This plant contains several types of bioactive compounds which exhibited significant antimicrobial activities (Li et al. 2009). Furthermore, a research demonstrated that hexan fraction of *E. spinidens* showed the inhibitory activity against HSV-1, and the IC<sub>50</sub> value of 9.92±0.072 mg/ml was determined (Li et al. 2009). Another study stated that the methanolic extract of *E. spinidens* was active against HSV-1 with EC<sub>50</sub> and SI values, of 0.34mg/ml and 14.9 respectively, and this Research showed that *E. spinidens* can inhibit the viral replication and adsorption (Karimi et al. 2016). *Ricinus communis* is another member of Euphorbiaceae family (Abdul et al. 2018), which contains many phytochemicals and can be used to treat a wide range of diseases (Scarpa and Guerci 1982; Ohishi et al. 2014). A study showed that ethanolic extracts of *R. communis* has potent antiviral activity against HSV-1 and inhibited this virus at concentration of 0.1 mg/ml (Abdul. et al. 1996).

### Fagaceae

*Quercus Persica*, commonly known as oak, belonging to the family Fagaceae, has been used in Iranian traditional medicine (ITM) for the treatment of various disease (Karimian et al. 2020). A study demonstrated that hydroalcoholic extract of *Q. Persica* has anti-HSV activity. In this research the authors conclude that *Q. Persica* extract has inhibited the HSV-1, and the IC<sub>50</sub> values, before and after attachment to BHK, were determined to be 1.02 and 0.257 µg/ml, respectively (Karimi et al. 2013). Another study by Karimi et al. stated that *Quercus brantii* extract showed the inhibitory activity against HSV-1, and the IC<sub>50</sub> and SI values of 4.3 µg/ml and 48.4 were determined, respectively (Karimi et al. 2017).

### Hypericaceae

*Hypericum perforatum*, a member of Hypericaceae family, is a medicinal plant which has been widely used as antidepressants, anti-cancer and psychotic disorders (Klemow et al. 2011). A number of studies demonstrated that *H. perforatum*, has strong antiviral activity against numerous viruses, including radiation-

leukaemia virus (RadLV), friend virus (FV), human immunodeficiency virus type 1 (HIV-1) and HSV-1 (Weber et al.1994). Also a scientific research showed that the complex of *H. perforatum* and lysine hydrochloride, remarkably inhibited the HSV-1 and the IC<sub>50</sub> value was from 6.8 to 9.7 mg/ml (HU et al. 2004).

### Lamiaceae

*Hyssopus officinalis* belongs to the family Lamiaceae, which is traditionally used for treatment of chest & lung conditions, coughs, colds and Infectious diseases (Vlase et al. 2014), also several studies demonstrated that *H. officinalis* extract has antifungal and antiviral activity (Fathiazad et al. 2011). A study by Behbahani, showed that methanolic extract of *H. officinalis* significantly inhibited two HSV serotypes, which the EC<sub>50</sub> and CC<sub>50</sub> values, against HSV-1, were determined to be 4.1±0.40 and 960 µg/ml, respectively, and for HSV-2, the EC<sub>50</sub> and CC<sub>50</sub> values were > 5.0 and 100 µg/ml, respectively (Behbahani 2009). Another study stated that essential oil of *H. officinalis* was active against HSV-1, and EC<sub>50</sub> and CC<sub>50</sub> values, were determined to be 0.0001±0.00001 and 0.0075±0.002 % respectively (Schnitzler et al. 2007). Another important species of Lamiaceae family is *Melissa officinalis*, which is a well-known and it has been used in traditional medicine for treatment of various diseases (Miraj et al. 2017). Furthermore, a research showed that *M. officinalis* has inhibitory activity against HSV-1 and inhibited the viral attachment to the host cells, and the IC<sub>50</sub> and SI values of 0.4 µg/ml and 350 were determined, respectively (Astani et al 2014). *Mentha piperita* is another important species of Lamiaceae family which has therapeutic potential to treat different diseases (Zaker et al. 2014; Alves et al. 2012). Schuhmacher et al., demonstrated that the essential oil of *M. piperita*, can able to inhibit the herpes simplex virus type 1, and reduce the plaque formation by up to 82% for HSV-1 (Schuhmacher et al. 2003). Another research stated that the *M. piperita* extract was effective against HSV-1 and inhibited the viral replication cycle, which ED<sub>50</sub> and TI values were determined to be 62.70 mg/ml and 1.79, respectively (Omidian et al. 2014). Several studies exhibited that many species of Lamiaceae family has potential to inhibit the two HSV serotypes. *Ocimum basilicum* or great basil, a traditional medicinal plant, belongs to the family Lamiaceae which is widely used for treatment of different diseases including, headaches, diabetes, nerve pain and anxiety (Bora et al. 2011). A study revealed that water and ethanolic extracts of *O. basilicum* have inhibited two HSV serotypes, the result of this research showed that the EC<sub>50</sub> and SI values of water extracts against HSV-1, were determined to be 90.9 mg/ml and 16.2, also for HSV-2 were 51.4 mg/ml and 28.6 respectively. Ethanolic extract showed inhibitory activity against HSV-1, and EC<sub>50</sub> and SI values of 108.3µg/ml and 6.3 were determined, respectively (Chiang et al. 2005). Another important

species of Lamiaceae family is *Rosmarinus officinalis*, which is widely used in treatment of rheumatic pain, headache, hysteria, stomachache, depression and infectious diseases (Ghasemzadeh Rahbardar et al. 2020). A study reported that extract of *R. officinalis*, exhibited potential antiviral activity against HSV-1 and HSV-2, which this extract at the concentration of 30 µg/ml inhibited the 55% of HSV-1 and at 40µg/ml inhibited the 65% of HSV-2 plaques and extract of *R. officinalis* showed the significant inhibitory effect at the 50 µg/ml concentration two HSV serotypes (Al-Megrin et al. 2020).

Another important species of Lamiaceae family is *Salvia officinalis*, that is used in traditional medicine to treat different kinds of diseases, such as rheumatism, diarrhea, ulcers, inflammation and paralysis. This plant contains several types of phytochemicals which exhibited significant antibacterial, antifungal and antiviral activities (Ghorbani and Esmailizadeh 2017). A study demonstrated that two diterpenoids compounds (saffinoline and sage one) which is isolated od aerial parts, have antiviral activity (Smidling et al. 2008). A number of research studies demonstrated that *S. officinalis* has antiviral activity against two serotypes of HSV. The extract of *S. officinalis* was used in the study, against HSV-1, which the IC<sub>50</sub> value of this extract, 199.0 µg/ml was determined (Smidling et al. 2008), and in another studies IC<sub>50</sub> value was 1.41–1.88 µg/ml and Inhibited the plaque formation (Santoyo et al. 2014). Schnitzler et al. studied the antiviral activity of *S. officinalis* extract against two serotypes of HSV which IC<sub>50</sub> values for HSV-1 and 2 were 0.18 and 0.04 µg/ml respectively (Schnitzler et al. 2008).

*Satureja hotensis* is another important species of Lamiaceae family which can use in treatment of many ailments and diseases. In this plant, various types of phytochemicals such as flavonoids steroids, triterpenoids, and and sesquiterpenoids, have been identified (Gursoy et al. 2009; Golestannejad et al. 2015), which are used in pharmaceutical industries (Tepe and Cilkiz 2016). A study showed that this plant has potential antiviral activity against HSV-1, which IC<sub>50</sub> and CC<sub>50</sub> values were determined to be 0.008% and 0.245%, respectively (Gavanji et al. 2015).

One of the important species of Lamiaceae family is *Thymus vulgaris* commonly known as thyme and is the rich sources of phytochemicals which are widely used for the treatment of inflammation, cancers, and infectious diseases (Gavanji and Larki 2017). A study demonstrated that the essential oil of *T. vulgaris* was effective against two serotypes of HSV and reduce the viral infectivity, which IC<sub>50</sub> for 1,8-cineole, 1200 µg/ml was determined (Gavanji and Larki 2017). Furthermore, a study revealed that aqueous extract of *T. vulgaris* has inhibitory effects against two serotypes of HSV, which IC<sub>50</sub> and SI values for HSV-1, were 0.065 mg/ml and 954, also for HSV-2, 0.077 mg/ml and 805 were

determined, respectively (Nolkemper et al. 2006). Another member of Lamiaceae family is *Thymus kotschyanus* which has anti-viral activity and inhibited HSV-1 at the higher concentration of 400 µg/ml (Farahani 2017). Based on a study, *T. kotschyanus* contains many bioactive compounds such as Borneol, has impressive antiviral potentials to inhibit herpes simplex viruses (Armaka et al. 1999) (Table 2). *Zataria multiflora* is one of the most important species of Lamiaceae family which is used to relieve some of illnesses such as fever, bone pain, flatulence, cough, cold and infectious diseases (Ghorani et al. 2022; Dadashi et al. 2016). A research study has been documented, reporting that methanolic extract of *Z. multiflora* at the 1000 mg/ml concentration, remarkably reduce the plaque formation of HSV-1 (Arabzadeh et al. 2013). Moreover, essential oil of *Z. multiflora* exhibited antiviral potential against HSV-1, in which IC<sub>50</sub> and SI values were determined to be 0.0059% and 11.7, respectively (Mardani et al. 2012). Another study revealed that essential oil of *Z. multiflora* contains Rosmarinic acid which is an antiviral compound and inhibited the viral attachment to host cells. this study demonstrated that *Z. multiflora* oil, has strong antiviral activity which IC<sub>50</sub> and CC<sub>50</sub> values were determined to be 0.003% and 0.166%, respectively (Gavanji et al. 2015). *Zingiber officinale* or Ginger is another important species of Lamiaceae family which is widely used for treatment different diseases in traditional medicine (Grzanna et al. 2005). *Z. officinale* has broad-spectrum antiviral potential on Human Respiratory Syncytial Virus (HRSV) (Chang et al. 2013), hepatitis C virus (HCV), influenza A (H1N1) (Sahoo et al. 2016), and two serotypes of HSV [123,180]. The study has demonstrated that *Z. officinale* inhibited the HSV-2 with IC<sub>50</sub> and SI values of 0.0001% and 40 respectively (Allahverdiyev et al. 2013). Another study by Koch et al stated that *Z. officinale* possess antiviral activity, and the IC<sub>50</sub> value of 0.001% was determined (Koch et al. 2008) (Table 2).

### Leguminosae

*Securigera Securidaca*, a species of Leguminosae family, is widely used as herbal for the treatment of several diseases in Iranian traditional medicine (ITM). *Securidaca* is a rich source of flavonoids having significant antibacterial, antifungal and antiviral activities (Raesi Vanani et al. 2019). Also the result of a research study showed that, two major compounds, including Kaempferol and kaempferol-7-O-glucoside which is isolated from *S. Securidaca*, can inhibit the HSV infection (Behbahani et al. 2013). Another study showed that methanolic extract of *S. Securidaca* has inhibited the HSV-2 with IC<sub>50</sub> and CC<sub>50</sub> values of 1.6 and 130 µg/ml, respectively (Sayedipour et al. 2012). Furthermore, *S. Securidaca* exhibited significant antiviral activity against HSV-1 which IC<sub>50</sub> and CC<sub>50</sub>



values of 2 and 500 µg/ml, were determined, respectively (Behbahani et al. 2013).

*Glycyrrhiza glabra* is another medicinal plant from Leguminosae family which has been reported for healing gastroesophageal reflux disease, liver diseases, tuberculosis and infectious diseases (Wahab et al. 2021). Numerous antiviral phytochemicals, such as glycyrrhetic acid, and glycyrrhizin were isolated from *G. glabra* which have antiviral activity against HSV-1 (Ming and Yin 2013; Huan et al. 2021). Based on the results of a research, *G. glabra* extract has inhibited the HSV-1 with IC<sub>50</sub> and CC<sub>50</sub> values of 500 and 800 µg/ml, respectively (Monavari et al. 2008). Another study by Fukuchi et al. stated that water extract of *G. glabra* with EC<sub>50</sub> and SI values of 650 to 740 mg/ml, and 2.0 to >4.6, respectively, showed a strong inhibitory activity against HSV-1, compared to alkaline extracts of *G. glabra* with EC<sub>50</sub> and SI values of 600 to >3000 mg/ml, and to 3.2, respectively (Fukuchi et al. 2016).

### Myrtaceae

*Eucalyptus caesia* and *Eucalyptus globulus* are the two most common species of Myrtaceae family which have Numerous phytopharmacological potential to treat different kinds of diseases, such as asthma, pulmonary, cold, bronchitis, and infectious diseases (Mieres-Castro et al. 2021). Both of these species exhibited antiviral properties against HSV-1 and HSV-2 (Mieres-Castro et al. 2021). A study demonstrated that essential oil of *E. globulus* inhibited two HSV serotypes which IC<sub>50</sub> and SI values for HSV-1, were determined to be 0.009% 3.3, respectively and for HSV-2, were 0.008% and 3.75, respectively (Schnitzler et al. 2001). Furthermore, a research demonstrated that 1,8-cineole reduced the HSV infection under in vivo condition (Behbahani et al. 2013). Another study Researchers compared the Effect of *E. globulus* oil and individual monoterpenes against HSV-1, which result of this study showed that *E. globulus* 1,8-cineole, α-pinene, γ-Terpinene, p-cymene, α-Terpineol and terpinen-4-ol, have antiviral activity against HSV-1 with IC<sub>50</sub> of 55, 1.20, 4.5, 7.0, 16.0, 22.0, and 60.0 µg/ml, respectively (Astani et al. 2010). Another study revealed that essential oil of *E. caesia* inhibited two HSV-1 which IC<sub>50</sub> and CC<sub>50</sub> values, were determined to be 0.004% and 0.287%, respectively (Gavanji et al. 2015).

*Myrtus communis* is another important member of Myrtaceae family, which has been used in traditional medicine to treat many diseases such as hemorrhoid, recurrent aphthous stomatitis, diarrhea, and infectious diseases (Mahboubi 2016; Alipour et al. 2016). Based on a study, the hydroalcoholic extract of *M. communis*, has impressive antiviral potentials to inhibit HSV-1, which IC<sub>50</sub> and CC<sub>50</sub> values, were determined to be 3100 and 4960 µg/ml, respectively (Moradi et al. 2011). This herb showed anti-herpetic activity, under clinical trial condition, which the result of this study demonstrated that myrtle oil, reduced the signs and symptoms of

disease in the treated group, in comparison to other control groups (Zolfaghari et al. 1997).

### Oleaceae

*Olea europaea*, a member of Oleaceae family, can be used to treat a wide range of diseases in traditional medicine, such as diarrhea, hemorrhoids, infectious diseases, inflammation and rheumatism (Alipour et al. 2016). *O. europaea* has antiviral activities against many types of viruses, including Canine parvovirus (CPV), hepatitis virus, bovine rhinovirus (BRV), herpes virus (HSV) and Feline leukemia virus (FeLV) (Ben-Amor et al. 2021). A study demonstrated that hydroalcoholic extract of *O. europaea* var. *sylvestris* exhibited anti-HSV-1 activity that EC<sub>50</sub> and CC<sub>50</sub> values, for pre-infection assay, were determined to be 0.12 and 0.2 mg/ml, respectively and for post-infection assay were 0.15 and 0.2 mg/ml, respectively (Ben-Amor et al. 2021). Another study by Motamedifar et al. stated that hydroalcoholic extract of *O. europaea* with IC<sub>50</sub> and CC<sub>50</sub> values of 660 and 1750 µg/ml, respectively, showed a strong inhibitory activity against HSV-1 (Motamedifar et al. 2015).

### Plantaginaceae

*Plantago major* belongs to the family Plantaginaceae, which is commonly known as greater plantain, and it has been traditionally used to treat many diseases such as fever, constipation and wounds and bleeding. Furthermore, *P. major* has been reported to contain caffeic acid, that demonstrated the strongest antiviral activity against two serotypes of HSV (Najafian et al. 2018). A study showed that aqueous extract of *P. major* has weak antiviral activity against HSV-1 and HSV-2, in extracts, pure compounds such as Caffeic acid demonstrated the strongest antiviral activity against HSV-1. Moreover, this study stated that aqueous extract of *P. major* inhibited HSV-2 with EC<sub>50</sub> and SI values, of 843 mg/ml and 2.2, respectively and Caffeic acid demonstrated the strongest antiviral activity against HSV-1. Moreover, this study stated that aqueous extract of *P. major* inhibited HSV-2 with EC<sub>50</sub> and SI values, of 843 mg/ml and 2.2, respectively and Caffeic acid isolated from *P. major* exhibited the antiviral activity against HSV-1 with EC<sub>50</sub> and SI values, of 15.3 µg/ml and 671, and HSV-2 EC<sub>50</sub> and SI values, were determined to be 87.3 µg/ml and 118, respectively (Chiang et al. 2002; Chiang 2003).

### Polygonaceae

*Rheum palmatum* a flowering plant of Polygonaceae family, which can be used to treat a wide range of diseases such as gastroenteric, herpes and kidney disease (Chang et al. 2014). *R. palmatum* contains several types of natural compounds such as emodin, chrysophanol and aloe-emodin which exhibited significant anti-viral activities (Li et al. 2007). A study has been documented that Aloe-emodin isolated from *R. palmatum* has antiviral activity against HSV (Types 1 and 2), influenza virus (Sydiskis et al. 1991), human cytomegalovirus (HCMV) (Barnard et al. 1992), and polio viruses (Semple et al. 2001), also emodin and

chrysophanol have antiviral property against hepatitis B virus (HBV) (Shuangsoo et al. 2006), hepatitis C virus (HCV) and human immunodeficiency viruses (HIV) (Kubin et al. 2005). A study demonstrated that *R. tanguticum* nanoparticles suppressed the HSV-1, which EC<sub>50</sub> and CC<sub>50</sub> values, were determined to be 194.1 and 415.3 µg/ml, respectively (Shen et al. 2019).

### Solanaceae

*Solanum paniculatum* or jurubeba, a member of Solanaceae family, which is widely used to treat several diseases including hypertension, anemia, inflammation and tuberculosis (Tenório et al. 2016). A research study by Valadares et al., showed that ethanolic extract of *S. paniculatum* exhibited antiviral property against HSV-1, which EC<sub>50</sub> and SI values, were determined to be 298 mg/ml and 1.4, respectively (Valadares et al. 2009).

### Theaceae

*Camellia sinensis* or green tea, is a medicinal plant of Theaceae family which is used as the most consumed and favorable drink in the world. *C. sinensis* has many medicinal properties (Singhal et al. 2017). Based on a study, *C. sinensis* contains many bioactive compounds that has impressive antiviral potentials to inhibit herpes simplex viruses tape 1, with IC<sub>50</sub> and SI values, of 20 mg/ml and 50, respectively (Farahani et al. 2014). Another study, stated that aqueous extract of *C. sinensis* exhibited the antiviral activity against HSV-1, which IC<sub>50</sub>, CC<sub>50</sub> and SI values, were determined to be 50, 1000 µg/ml and 20, respectively (Farahani et al. 2013) Another scientific research reported that methanolic extracts of *C. sinensis* completely inhibited two HSV serotypes at 12 µg/mL concentration (Deepika et al. 2014).

### Xanthorrhoeaceae

*Aloe vera*, commonly known as *Aloe barbadensis*, is a member of Xanthorrhoeaceae family which has been traditionally used to treat various diseases such as abdominal pains, malaria, arthritis, fever, and skin diseases (Adams et al. 2014). *A. vera* produces a wide range of phytochemicals, such as emodin and Aloe-emodin which exhibit potential strong antiviral activity against two serotypes of HSV, immunodeficiency virus (HIV), and influenza virus (brahimi et al. 2021). Another an anthraquinone compound isolated from *A. vera*, is Aloe-emodin which inhibits the viral replication of HSV serotypes and the IC<sub>50</sub> value, of 1.5–6.0 µg/mL was determined (Sydiskis et al. 1991). A study demonstrated that topical *A. vera* gel at 0.2 to 5% concentrations can inhibit HSV-I growth (Rezazadeh et al. 2016). Another study by Ebrahimi et al. revealed that *A. vera* extract inhibited the HSV-1 with IC<sub>50</sub>, CC<sub>50</sub> and SI values, were determined to be 10000 ± 55, 20000 ± 94 µg/ml, and 2.0 respectively (brahimi et al. 2021). Also the result of a study showed that hot glycerine

extract of *Aloe vera* can able to inhibit the HSV-2, which the IC<sub>50</sub>, CC<sub>50</sub> and SI values, were determined to be 428, 3238 µg/ml and 7.56, respectively (Zandi et al. 2007).

### Zingiberaceae

*Curcuma longa* belongs to the family Zingiberaceae, which is used in Iranian traditional medicine (ITM) for healing rheumatism, anorexia, wounds, cough and respiratory diseases (Trujillo et al. 2013). A research study showed that, 2 mg/mL of *C. longa* extract reduced the plaque formation of HSV-1 (Fani et al. 2015). Furthermore, a research demonstrated that *C. longa* has inhibitory effect against HSV-1, and the IC<sub>50</sub>, CC<sub>50</sub> and SI values were 33.0, 484.2 µg/ml and 14.6, respectively (Lyu et al. 2005). Another study revealed that *C. longa* extract contains polyphenolic compounds such as Curcumin which affects the viral transactivator protein VP16 -mediated recruitment of RNA polymerase II (Pol II) to Immediate early (IE) gene promoters and Inhibits the HSV-1 replication. This study stated that curcumin has significant antiherpetic activity and inhibited HSV-2 with ED<sub>50</sub> value, of 0.32 mg/ml (Kutluay et al. 2008). *Zingiber officinale* or ginger is another antiviral species of Zingiberaceae family which exhibited antiviral activity against numerous viruses (Wang et al. 2020). Based on a study, the essential oil of *Z. officinale*, has impressive antiviral potentials to inhibit HSV-1, whit IC<sub>50</sub> value, of 0.001% (Koch et al. 2008).

## CONCLUSIONS

Since time immemorial, a human being has sought medications to relieve pain and remedy for various diseases. Weighty evidence demonstrates the use of medicinal plants for therapeutic purposes and numerous research studies have been done to investigate the novel antiviral agents. In this review, all reported data of herbal medicines (34 herbs from 17 families) with antiviral activity against HSV through Iranian Herbal Pharmacopoeia (IHP) were collected. In some cases, screening test of medicinal plants for anti-herpetic activity was done under in vitro condition and only a few of them were done under clinical trial condition. Additionally, in many research studies, bioactive phytochemicals and mechanisms of actions, were not identified. Results of this review suggest that further research to identify and purify the bioactive compounds to determine the molecular mechanisms of action are needed.

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