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ANTIVIRAL AND IMMUNOMODULATORY ACTIVITIES OF GENUS *SAUSSUREA* (ASTERACEAE): A REVIEW

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Asteraceae (Compositae) family has a crucial role in complementary and alternative medicine, with its plants known for their biological applications and high economic value. Since ancient times, these plants, such as those in the Saussurea genus, have been used for treating various diseases. Throughout the ages, Saussurea species have attracted attention for their therapeutic abilities and the importance of their many biological applications. Therefore, this is the first review with the aim of demonstrating the antiviral activity and immunomodulator effects of Saussurea species. We investigated a wide range of literature across the biggest scientific databases to obtain the necessary information about the plants of Saussurea genus and their biological applications. We found that many Saussurea species have antiviral activity against various viruses, including enveloped single-stranded RNA viruses, whether negative-sense or positive-sense, and also have antiviral activity against enveloped double-stranded DNA viruses. We also found that the scientific papers indicated many immunomodulator agents that were isolated from different Saussurea species. These findings support the significance of Saussurea species as a potential source of medications for the immune system and as efficient antiviral drugs. These plants may possibly be useful in future virus-caused pandemics as a primitive and complementary method of disease management. Some of these plants need further investigations and studies to prove their antiviral activity clearly and, in addition, to discover more Saussurea species that likely possess antiviral or immunomodulatory properties.

Keywords: *Asteraceae, Saussurea, Antiviral, Immunomodulator, RNA virus, DNA virus*

INTRODUCTION

One of the largest genera in the Asteraceae tribe, Cardueae, is *Saussurea*, which contains over 493 species[1] with a geographical distribution throughout the temperate regions of Asia, Europe, America, and Australia[2-5]. The majority of the species in this genus are found in Central and Eastern Asia, which is also the area with the greatest diversity of species[6, 7]. More than 10 *Saussurea* species have been used for a very long time in Chinese folk medicine, and about 30 of them have been utilized in traditional Chinese medicine (TCM)[8,9]. For instance, the Southwest Chinese plant *Saussurea lappa* exhibits spasmolytic, antihypertension, and antimicrobial properties[10]. *Saussurea costus* herb with flower is involved in a Chinese formulation for improving bodily immunity and can strongly treat premature ovarian failure[11]. The biological properties of *Saussurea pulchella* include anti-inflammatory, anti-hypertension, anti-hepatitis, and anti-arthritic effects. It has been used as a folk remedy in Korea[12,13]. Lower abdominal pain and rheumatoid arthritis have both been treated with *Saussurea involucrata*, a priceless traditional Chinese medicine[14]. As a traditional Korean medicine, *Saussurea triangulata* is used to cure hepatitis, hypertension, and inflammation. The rhizome of *S. petrovii* was

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used to treat bleeding and rheumatism in the past[15]. The Chinese plant *Saussurea medusa*, which is native to the Tibetan Plateau, is mainly employed to treat rheumatoid arthritis, gynaecology, and to increase physical endurance[16-19]. Sesquiterpenes, triterpenes, flavonoids, lignans, and phenolic chemicals are the main chemical components of this genus' plants[20].

Interest in *Saussurea* species has increased in recent years due to the discovery of various biological activities, including immunostimulants, which have opened up new research and therapeutic possibilities.[21-23] and antiviral properties[24-26]. Phytochemicals like flavonoids, terpenoids, and lignans have been found to have therapeutic properties against various viruses. Preliminary studies in experimental models show the protective impact of plant-derived natural chemicals against viral infection [27-31].

In this article, we have made an attempt to thoroughly review and provide an extensive description of several phyto-antiviral and immunostimulant agents from *Saussurea* species. In addition, to supply crucial information that promotes the implementation of extensive clinical trials and the justification of a medicinal application of these species.

MATERIAL AND METHODS

The authors conducted an electronic literature search to gather primary studies on the *Saussurea* genus using the following online databases: Science Direct (http://www.sciencedirect.com), Scopus (www.scopus.com), PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Wiley Online Library (http://onlinelibrary.wiley.com/), in addition to Web of Science (http://apps.webofknowledge.com), Taylor and Francis (https://www.tandfonline.com/), Google Scholar (http://scholar.google.com), Baidu Scholar (https://xueshu.baidu.com/), and CNKI (https://www.cnki.net/index/). The search employed relevant keywords, namely "*Saussurea*", "Antiviral", and "Immunomodulator" as search items indicated in the title, abstract, and keywords without specific language limitation or time limit. The current review includes references to new research findings, review papers, magazine articles, book references, local records, classical Chinese herbal literature, and PhD and MSc dissertations.

RESULTS AND DISCUSSION

Antiviral activity of *Saussurea* genus plants

Antiviral activity against enveloped, negative-sense, single-stranded RNA viruses

Influenza Virus

Numerous phytochemicals treat a variety of disorders because they are easily accessible, inexpensive[32]. Two compounds, Arctiin and chlorojanerin were obtained from extract of *Saussurea heteromalla*[33]. In the literature, chlorojanerin **(1)** is a sesquiterpene lactone in **Fig. 1** has been studied for its antiviral and anti-ulcer properties[34]. Arctiin **(2)** is a lignan as shown in **Fig. 1** present in several plants belonging to the Asteraceae family[35]. Arctiin is an influenza therapeutic agent that protects against lethal influenza virus (IFV), inhibits viral replication, improves immunological response, and reduces drug-resistant virus generation. Its effectiveness is enhanced with oseltamivir, and when combined with oseltamivir, it significantly reduces virus yields in bronchoalveolar lavage fluids and the lungs[36].

A study evaluated 43 methanolic extracts from 41 plant species for antiviral activity against influenza virus A, whose life cycle is shown in **Fig. 2.** *Saussurea auriculata* extract was found non-toxic to Madin-Darby canine kidney (MDCK) cells at 100 μgml^{-1} and moderately effective against influenza virus A (IC_{50} value 42 μgml^{-1}), suggesting the genus *Saussurea* could be a potential source of antiviral agents[37]. The bioactive components at their low concentrations in the extract show moderate antiviral activity[38].

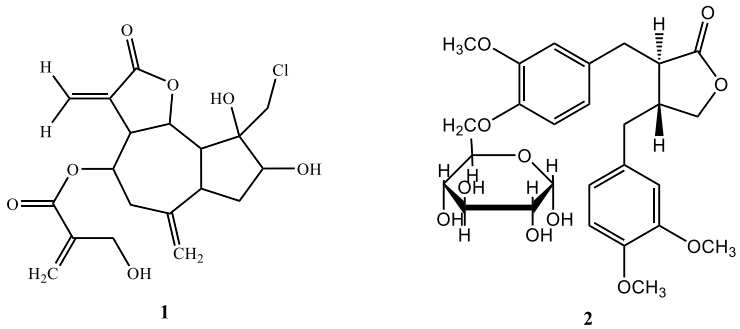
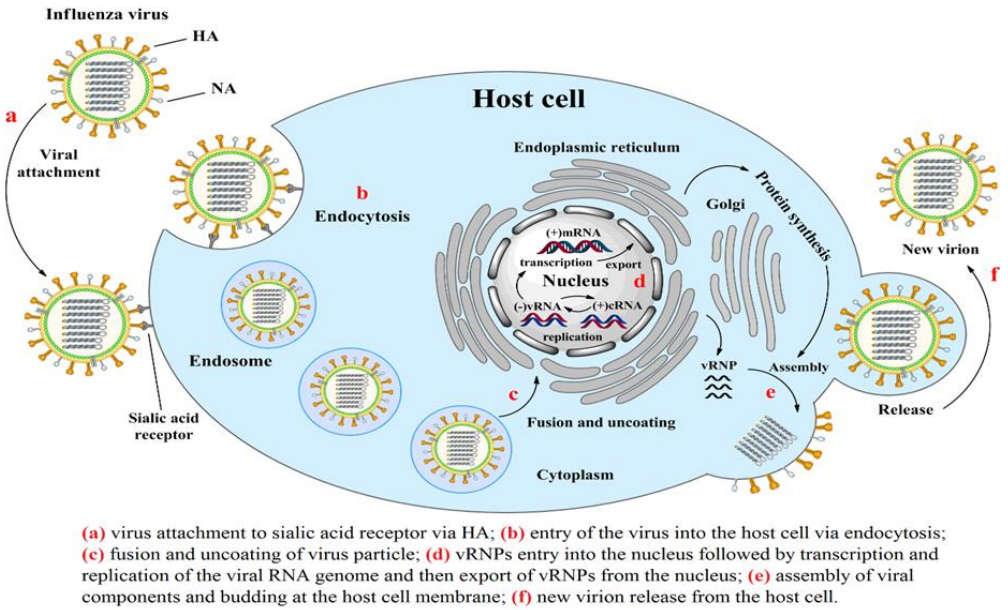


Fig. 1: Antiviral agents from *Saussurea* genus: Chlorojanerin **(1)**[33] – Arctiin **(2)**[35] are two antiviral compounds extracted from *S. heteromalla*.



(a) virus attachment to sialic acid receptor via HA; (b) entry of the virus into the host cell via endocytosis; (c) fusion and uncoating of virus particle; (d) vRNPs entry into the nucleus followed by transcription and replication of the viral RNA genome and then export of vRNPs from the nucleus; (e) assembly of viral components and budding at the host cell membrane; (f) new virion release from the host cell.

Fig. 2: The life cycle of influenza A virus**.**

Spring viraemia of carp virus (SVCV)

Arctigenin (ATG), an aglycone found in *Saussurea medusa*, has been used for modifications. ATG's derivative, 4'-(8-imidazole-octyloxy)-arctigenin (6A), demonstrated strong activity against SVCV, with an IC_{50} of 0.095 μg/mL. The synthetic route of 6A, an immunosuppressive drug, with the required reagents and conditions is shown in **Fig. 3. 6A** reduced SVCV replication in Endothelial progenitor cells (EPC) at a concentration of 10 mg/L[39]. Zebra fish treated with 6A showed no significant interferon response against SVCV infection, and immune gene expression was reduced in EPC treated with 6A alone. When 6A was given 1 h after virus infection, it demonstrated strong anti-SVCV activity. 6A mainly inhibited the early events of the replication cycle of SVCV, which was estimated to take about 8 hours[40]. 6A treatment could increase survival rates while decreasing viral load[41]. Coumarin derivative, 7-(6-(2-methyl imidazole))-coumarin, effectively prevents rhabdovirus infection in fish, reducing mortality by 22.5% in zebrafish infected with SVCV after activating the fish interferon response[42]. 7-[6-(2-methylimidazole) hexyloxy] coumarin altered the structure of the SVCV glycoprotein, preventing viral binding to surface of cell or translocation to the cytosol[40]. Another coumarin derivative, 7-(4-benzimidazolebutoxy)-coumarin, has been shown to increase HO-1 expression and decrease SVCV replication via PKCα/β-Nrf2 signaling[43].

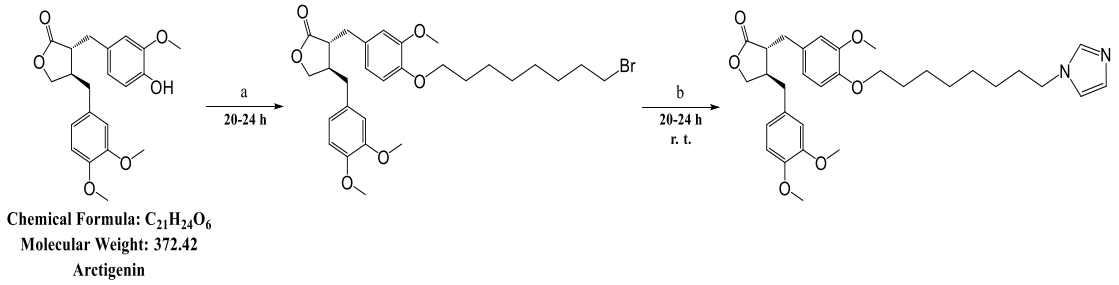


Fig. 3: Synthesis of 4′-(8-imidazole-octyloxy)-arctigenin: (a) alkyl dibromide, K_2CO_3, dry acetone, reflux; (b) imidazole, K_2CO_3, CH_3CN [44].

Infectious hematopoietic necrosis virus (IHNV)

Infectious hematopoietic necrosis virus (IHNV) is a type of RNA virus in the Rhabdoviridae family, as listed in **Table 1.** 4-(8-(2-ethylimidazole)octyloxy)-arctigenin (EOA), an arctigenin derivative whose synthetic route with required reagents and conditions is shown in **Fig. 4**. EOA is stable and has a prolonged inhibitory half-life during an early viral infection. It suppresses IHNV glycoprotein (G) gene expression in virus-sensitive organs like the kidney and spleen. EOA's 72-hour IC_{50} on G was 1.15 mg/L, and it demonstrated high antiviral activity against IHNV at 2 mg/L, with a maximal inhibition rate over 90%. *In vivo*, EOA treatment increased the survival rate of infected rainbow trout by 32.0%[45]. Autophagy activation suppressed both IHNV extracellular viral output and intracellular viral replication when EPC were infected with IHNV. EOA's antiviral mechanism could be similar to that of rapamycin, an autophagy inducer[46] that has been shown to inhibit *IL-8*, *IL-12p40*, and *TNF- α* [47, 48]. According to the findings, EOA has the potential to be a treatment for IHNV infection in aquaculture[45].

Table 1: Antiviral activity of *Saussurea* plants against enveloped, negative-sense, single-stranded RNA viruses.

Virus	Family	Antiviral agent	Source	Chemical class.	References
Lethal influenza virus (IFV)-infection	Orthomyxoviridae	Arctiin	Ethyl acetate soluble fraction of dichloromethane : methanol (1:1) extract of *Saussurea heteromalla*	Lignan	33, 34, 35
Influenza Virus A	Orthomyxoviridae	–	Methanolic extract of *Saussurea auriculata*	–	36, 37
H9N2 avian influenza viruses (AIVs)	Orthomyxoviridae	Arctiin	–	Lignan glycoside	49
Spring viraemia of carp virus (SVCV)	Rhabdoviridae	Arctigenin derivative Coumarin derivatives	–	Lignan Benzopyrones	39, 44 40, 42, 43
Infectious hematopoietic necrosis virus (IHNV)	Rhabdoviridae	Arctigenin derivative	–	Lignan	45-46
Ranikhet- disease virus	Paramyxoviridae	–	*Saussurea obvollata* flower extract	–	50

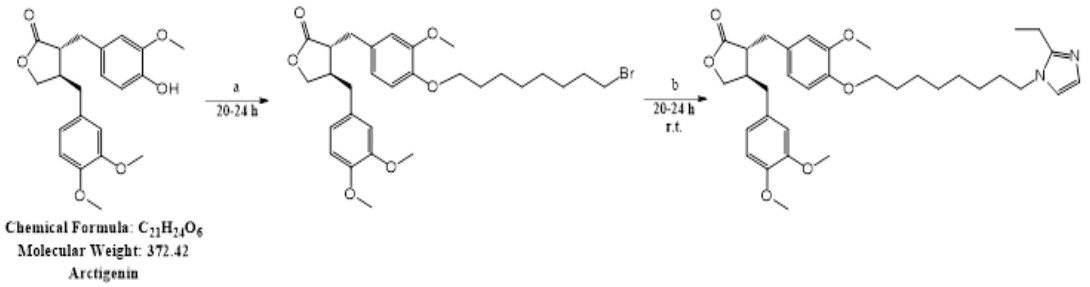


Fig. 4: Synthesis of EOA: (a) 1,8- dibromooctane, K_2CO_3, dry acetone, reflux; (b) 2-ethylimidazole, K_2CO_3, CH_3CN [45].

Antiviral activity against enveloped, positive-sense, single-stranded RNA viruses

Japanese encephalitis virus (JEV)

Arctigenin (AR), an aglycone found in Saussurea medusa, was found to be effective in treating Japanese encephalitis virus (JEV) in mice of either sex. The study involved a lethal dose of JEV given intravenously to four to five-week-old BALB/c mice, followed by arctigenin intraperitoneally twice daily for seven days. All untreated animals died on the 9th day after infection; however, arctigenin treatment offered full protection in both in vivo and in vitro studies. Arctigenin's neuroprotective effect was associated with decreased viral load, neuronal death, active caspase-3 activity, reactive oxygen species, levels of stress-associated signaling molecules, and TNF-alpha production. This reduced inflammatory responses and established its potential for treating inflammation-related complications[51, 52]. Additionally, arctigenin treatment improves the behavioral outcome after JE. Arctigenin's antiviral, neuroprotective, anti-inflammatory, and antioxidative properties effectively reduced the severity of JEV-induced disease[51].

Hepatitis C virus (HCV)

To develop novel anti-hepatitis C virus (HCV) drugs from natural resources, 93 Yunnan crude drugs were investigated, including the whole plant of *Sausurea namikawae* Kitam. and *Saussurea laniceps* Hand.-Mazz., as mentioned in **Table 2**. They were evaluated for their inhibitory effect on NS5B protein, which is recombinant HCV RNA-dependent RNA polymerase (RdRp). There were some extracts with significant tannin content. The majority of crude drugs were reported to contain a variety of tannins, which bind to proteins and have an inhibitory impact on the HCV-RdRp enzyme. The aqueous extracts of *Sausurea namikawae* Kitam. have inhibitory activity on HCV-RdRp by 57.9% with IC_{50} 28.8 µg/ml and <0.5% of tannins content. While *Saussurea laniceps* Hand.-Mazz. aqueous extracts inhibit HCV-RdRp by 55.8% with IC_{50} 35.0 µg/ml and <0.5% of tannins content[53].

SARS-CoV-2 (COVID-19)

Since December 2019, the novel coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 from the Coronaviridae family, has been a global health problem[54,55], a spherical enveloped virus with a single-stranded RNA genome, as shown in **Fig. 5** [56, 57]. Lupeol **(3)**, shown in **Fig. 6**, is a triterpenoid found in *S. lappa* (syn. *S. costus* and *Aucklandia costus*). It has high affinity in silico studies to target the spike (S) protein of SARS-CoV-2 proteins[58]. Myrcene in *S. costus*, which may inhibit viral entry of SARS-CoV-2 into cells by its potential to interfere with angiotensin-converting enzyme (ACE) receptors[59]. In folk medicine, *S. costus* is commonly used in the treatment of a variety of diseases, such as fever, headache, cough, bronchial asthma [60, 61, 62, 63, 64, 65], and viral infection due to lupeol, p-cymene, tannins, stigmasterol, and botulin in *S. costus*[66]. *S. costus* also has antimicrobial and antibacterial properties and inhibits the cyclooxygenase (COX) enzyme, which reduces pain and inflammation [67-70]. All of this information suggests that *S. costus* might be helpful in the treatment of COVID-19 disease[71]. Unani medicine prioritizes three measures during outbreaks: environmental purification using herbal drugs such as *Saussurea costus* Falc.

Lipsch. (Qust) as sprays or fumigants, health promotion and immune modulation, and the use of health-protective and symptom-specific drugs[72-74]. The using of *Saussurea costus* for the sanitization due to its insect repellant activity and toxicity[75]. The GC-MS analysis of *S. costus* extract revealed 69 chemical components, including terpenoids, hydrocarbons, sterols, alkaloids, and phenolic compounds. The extract showed significant antiviral activity against herpes simplex virus 1 (HSV-1) but no effect on SARS-CoV-2 entry prevention[76].

Idriss' investigation identify 48 substances in *S. costus* extract using gas chromatography-mass spectrometry (GC-MS), with fatty acids showing the highest abundance (73.8%). Of these substances, 22 were docked on the catalytic dyad of His41 and Cys145 on the active side of the main SARS-CoV-2 protease (M^{pro}). The most effective inhibitors shown in **Fig. 6** are 4,8,13-Cyclotetradecatriene-1,3-diol,1,5,9-trimethyl-12-(1-methylethyl) **(4)**, andrographolide **(5)**, as well as delta 4-androstene-3.beta,17.beta-diol **(6)**. The binding affinity of **(6)** ranged from −6.1 to −6.5 kcal/mol[77]. A study on 10 adult female K18-hACE2 transgenic mice found that the extract of *S. lappa*, which possesses antiviral properties, protected them from weight loss and viral replication in a challenge test against SARS-CoV-2. The results showed that the extract-treated mice had healthier lungs and were able to survive in the experiment[24].

The Alpha Variant of Concern (VOC), also known as Kent VOC or S gene negative, was replaced by the Delta VOC on May 19, 2021[78]. Houchi et al. conducted in-silico screening of 55 bioactive constituents from *Saussurea costus* and *Saussurea involucrata* to find inhibitors of two viral proteases, M^{pro} (PDB ID: 6LU7) and RBD of SGP of SARS-CoV-2 (B1.617.2). Tangshenoside III, Rutin, and Hesperidin generated stable complexes and displayed remarkable binding energies in the following order: Tangshenoside III, Rutin, and Hesperidin (−9.07, −7.71, and −7.57 kcal/mol) with M^{pro} and Rutin, Tangshenoside III and Hesperidin (−9.07, −7.71, and −7.57 kcal/mol) with RBD of SGP. These substances are not carcinogenic or mutagenic. Rutin was the most reactive of the three inhibitors against B1.617.2 Delta and M^{pro}, suggesting it may be a candidate for an antiviral drug[26].

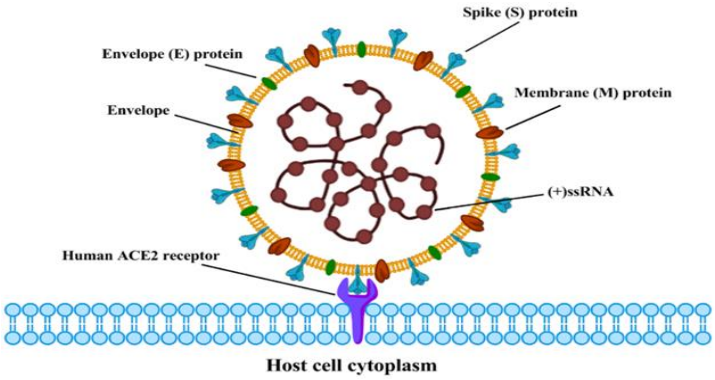


Fig. 5 : SARS-CoV-2 (COVID-19) and its target proteins and its mechanism of host entry.

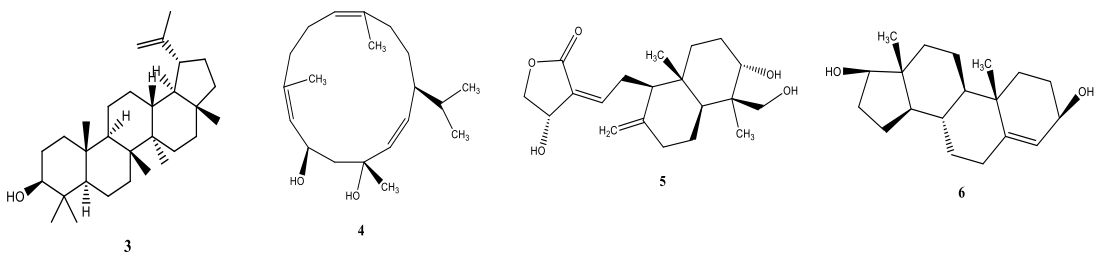


Fig. 6 : Antiviral agents from *Saussurea* genus: Lupeol **(3)**[87] – 4,8,13-Cyclotetradecatriene-1,3-diol,1,5,9-trimethyl-12-(1-methylethyl) **(4),** Andrographolide **(5),** Delta 4-androstene-3.beta,17.beta-diol **(6)** are COVID-19 inhibitors extracted from *S. costus*[77].

Table 2 : Antiviral activity of Saussurea plants against enveloped, positive-sense, single-stranded RNA viruses.

Virus	Family	Antiviral agent	Source	Chemical class.	Effect/Mechanism	References
Japanese encephalitis virus (JEV)	Flaviviridae	Arctigenin	*Saussurea medusa*	Lignan	–	51, 88
Hepatitis C virus (HCV)	Flaviviridae	–	Aqueous extract of *Saussurea namikawae* & *Saussurea laniceps*	–	Tannins bind to proteins and have an inhibitory impact on the HCV-RdRp enzyme.	53
SARS-CoV-2 (COVID-19)	Coronaviridae	lupeol	*Saussurea costus* Falc. Lipsch. Roots (Qust)	Triterpenoid	Targets coronavirus spike protein.	54
		Myrcene		Monoterpenes		59
		P-cymene, tannins, stigmasterol, and botulin				66
					Sanitization of the environment by fumigation because *S. costus* is used as an insect repellant and toxic.	72
Human Immunodeficiency Virus Type-1 (HIV-1)	Retroviridae	(-)-Arctigenin	*Saussurea medusa*	lignanolide	Prevent the integration of proviral DNA into the cellular DNA genome in human cells.	79, 80, 81, 83, 86
HIV and Other Retroviruses	Retroviridae	n-Docosanol	*Saussurea obvallata*	Saturated 22-carbon aliphatic alcohol	–	89

Inhibitors of Human Immunodeficiency Virus Type-1 Integrase

The study examined the effectiveness of (-) -arctigenin, a lignanolide from *Saussurea medusa*, and 27 related lignans in preventing 3'-processing and strand transfer by immunodeficiency virus type 1 (HIV-1) integrase. Arctigenin inhibits HIV replication but is ineffective against HIV-1 integrase. Arctigenin-related derivatives, mentioned in **Fig. 7**, showed activity, with some showing 100% inhibition, such as (2R,3R)-2,3-Bis(3,4-dihydroxybenzyl)butyrolactone**(7)**,(2R,3R)-2-(3',4'-Dihydroxybenzyl)-3-(3",4"dimethoxybenzyl)butyrolactone **(8)**, and (2R,3R)-2-(4'-Hydroxy-3'-methoxybenzyl)-3-(3",4"-dihydroxybenzyl)butyrolactone **(9)**. The anti-HIV-1 action of (-)-arctigeninmay be due either to its metabolism of certain O-demethylated congeners with HIV-1 integrase-inhibiting action or to its activity in an earlier phase in the life cycle of the virus[79-83].

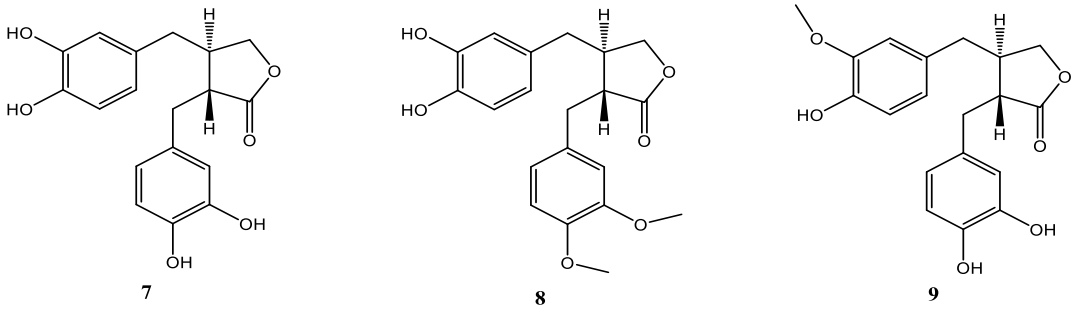


Fig. 7 : Antiviral agents from *Saussurea* genus: (2R,3R)-2,3-Bis(3,4-dihydroxybenzyl)butyrolactone **(7)**, (2R,3R)-2-(3',4'-Dihydroxybenzyl)-3-(3",4"-dimethoxybenzyl)butyrolactone **(8)**, (2R,3R)-2-(4'-Hydroxy-3'-methoxybenzyl)-3-(3",4"-dihydroxybenzyl)butyrolactone **(9)** are arctigenin's derivatives act as HIV type 1 inhibitors [79].

HSV-1, HSV-2, Varicella zoster virus (VZV), Cytomegalovirus (CMV), Human Herpesvirus 6 (HHV-6), and HIV-1 are all inhibited by docosanol *in vitro*, which isolated from *Saussurea obvallata*[84, 85]. A study on ten HIV-1-infected patients treated 28 cutaneous Kaposi's sarcoma (KS) lesions with docosanol 10% cream for four weeks. After an extended treatment program, for all target lesions, the average percent decrease in lesion area was 20% ($p < 0.01$). The anti-HIV regimen, HIV viral level, and past KS therapies did not affect medication response. Docosanol is suggested as a possible topical therapy for AIDS-related Kaposi's sarcoma lesions[86].

Antiviral activity against enveloped, double-stranded DNA viruses

Hepatitis B virus (HBV)

SLP-4 is a typical pectin polysaccharide isolated from the petal of Saussurea laniceps. SLP-4 has anti-virus action against the hepatitis B virus (HBV) because of its structure-function relationship. Rhamnogalacturonan I (RG-1) had interaction with Hepatitis B envelope antigen (HBeAg) or Hepatitis B surface antigen (HBsAg)[25], so that it could efficiently suppress the HBV secretion through the interaction between HBV proteins and SLP-4. SLP-4 effectively inhibited HBV proliferation in HepG2.2.15 cells without cellular pathways, preventing the release of HBsAg and HBeAg, and had a minimal impact on HBV DNA replication[25, 90]. SLP-4's effects on HBeAg secretion were noticeably better than those on HBsAg secretion in this investigation, suggesting that SLP-4's anti-HBV mechanism may differ from that of other polysaccharides with anti-HBV properties[91]. Experimental medications significantly impacted HBV expression in HepG2.2.15 cells. SLP-4 and 3TC treatment (lamivudine is a common therapy for HBV and can inhibit HBV replication) significantly reduced HBsAg and HBeAg secretion, with most antiviral medications and polysaccharides inhibiting HBsAg more potently than HBeAg[92-95]. This study suggests that SLP-4's anti-HBV mechanism may be shared by other polysaccharides, offering new insights into their antiviral activity and potential applications in food preparation and drug delivery[25].

The secondary metabolites dehydrocostus lactone **(10)** and costunolide **(11)** mentioned in **Fig. 8** were isolated from *S. costus* roots, one of the Indian medicinal plants (AYUSH), and showed antiviral activity towards HBV by significantly suppressing the expression of HBsAg with IC_{50} (1.0 and 2.0 µM) in a dose-dependent manner in human hepatoma Hep 3B cells[96, 97]. The alcoholic extract of *Saussurea lappa* roots inhibits HBsAg formation in Hep3B cells with IC_{50} of 1.0–2.0 µM and Hep A2 cells. Both costunolide and dehydrocostus lactone reduce HBsAg gene expression at the mRNA level. They also inhibit HBsAg and HBeAg in HepA2 cells, suggesting the potential development of costunolide and dehydrocostus lactone as anti-HBV medicines[69, 98, 99, 100]. Several studies have shown that the unsaturated carbonyl group in the α-methylene-γ-butyrolactone moiety of costunolide and dehydrocostus lactone may

have an important role in cell biology by conjugating with target protein mercapto (SH)-groups[99, 101]. The study evaluated the potency of the crude extract of *Saussurea lappa* in suppressing HBsAg and HBeAg in chronic hepatitis B (CHB) patients. The patients were given 15 mL of *S. lappa* decoction and 15 mL of *Artemisia absinthium* decoction daily for 12 weeks. The drug significantly decreased HBV DNA, HBsAg, and HBeAg while improving liver functions without any side effects[102].

Herpes Simplex Virus (HSV)

Herpes simplex virus infections impact people around the world. The virion is constructed up of a nucleocapsid holding the viral DNA[103, 104]. Antiviral treatment may lower morbidity and mortality, but its effectiveness remains contentious[105]. Recurrent herpes labialis (RHL) or herpes simplex labialis (HSL) is a severe oral infection affecting 20%–40% of adults. It is caused by the HSV-1 neurotropic DNA virus[106-108]. HSV-1 infection prevalence in 2015–2016 was 47.8% in the US and 63.6% worldwide. Oral-to-genital infections are more common but have a lower reactivation probability[109].

HSL, often known as fever blisters or cold sores, is a chronic oral-facial condition that can be treated with docosanol **(12)**, which is shown in **Fig. 8** [107, 110]. Systemic antiviral treatment for HSL aims to decrease viral DNA production without affecting host function, focusing on acyclovir (ACV), a high-safety medication used for nearly three decades[105]. Docosanol, a novel antiviral drug, differs from existing nucleoside analogues by preventing HSV-1 entry into host cells and herpes virus replication both *in vitro* and *in vivo*[85, 111]. Docosanol inhibits the development of mutant viral strains that are resistant to the drug, as summarized in **Table 3**. The only over-the-counter medication for treating HSL that has been approved by the US Food and Drug Administration (FDA) is topical docosanol as an alternative to topical penciclovir and acyclovir[112, 113]. Docosanol significantly enhances the effectiveness of ACV against all tested herpesviruses, potentially affecting other viruses like ACV-resistant HSV mutants, HIV, influenza, respiratory syncytial virus, and vaccinia virus. In human peripheral blood mononuclear cells, docosanol prevents HIV and human herpesvirus-6 replication[89, 114]. Docosanol's action relies on its permeation through human cadaver skin. A vertical Franz diffusion cell was used to investigate this process[115]. N-docosanol inhibits the fusion of the HSV and preventing the generation of intermediate early gene products. Its antiviral properties require a time-dependent metabolic change. Cellular resistance to infection reduces after a $t_{1/2}$ of about 3 hours, and n-docosanol reduces viral gene expression by 70% and inhibits the release of virion-associated regulatory molecules[116]. Alantolactone **(13)**, which is demonstrated in **Fig. 8**, is a sesquiterpene lactone found in *Saussurea costus* extract[117]. The study examined the effects of alantolactone on HSV-1 using an MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) assay and a cytotoxic effect (CPE)-based assay. Alantolactone may have less potent antiviral activity at 10^{-6} g/mL due to its cytotoxic effect on Vero cells[118].

Immunomodulatory activity of *Saussurea* genus plants Curcumene

The relative percentage of total aromatic sesquiterpene compounds detected in hexane extract of Egyptian marketed *Saussurea* costus (Falc.) Lipsch. root powder was 0.66% , methylated fraction was 0.39%, and Solid-phase microextraction (SPME) extracted oil using GC – MS was 5.83%. The most representative compound in this class of compounds is curcumene. Because of their lower molecular weight, the SPME method produced the highest yield (5.83%) of various isomers of curcumene (α-Curcumene, β-Curcumene, γ-Curcumene). Curcumene has a wide range of pharmacological properties, including immunomodulation[121]. Hydrodistillation of Chinese costus oil produced a lower yield of curcumene (4.3%)[122, 123].

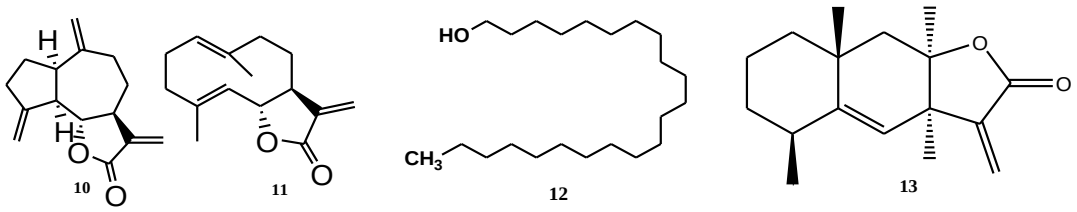


Fig. 8 : Antiviral agents from *Saussurea* genus: Dehydrocostus lactone **(10),** Costunolide **(11)** are secondary metabolites isolated from *S. costus* roots and showed antiviral activity against HBV[98]. Docosanol **(12)** from *S. obvallata* showed antiviral activity against HSV-1 [119].
Alantolactone **(13)** from *S. costus* showed antiviral activity against HSV-1[117].

Table 3: Antiviral activity of *Saussurea* plants against enveloped, double-stranded DNA viruses.

Virus	Family	Antiviral agent	Source	Chemical class.	Effect/Mechanism	Re.
Hepatitis B virus (HBV)	Hepadnaviridae	Pectin polysaccharide (SLP-4)	The petal of *Saussurea laniceps*	Polysaccharide	RG-1 had interaction with HBeAg or HBsAg, effects of SLP-4 on HBeAg secretion were noticeably better than those on HBsAg secretion.	25, 91, 120
		Costunolide & dehydrocostus lactone	*Saussurea costus*	Sesquiterpene lactones		69, 98-100
			Decoction of the crude root of *S. lappa* (qust)		Decrease HBV DNA, HBsAg, and HBeAg while also improving liver functions with no noticeable side effects.	102
			Hexane fraction of alcoholic extract of *Saussurea lappa*		Hexane fraction of alcoholic extract of *Saussurea lappa* roots inhibits HBsAg formation by Hep3B cells with IC_{50} of 1.0–2.0 µM	96
Herpes simplex virus (HSV)	Herpesviridae	n- docosanol	*Saussurea obvallata*	Saturated 22-carbon aliphatic alcohol	Inhibits the fusion of the HSV envelope and plasma membrane.	114, 116
HSV-1	Herpesviridae	Alantolactone	*Saussurea costus*	Sesquiterpene lactone	Significantly inhibited viral infection at 10^{-7} g/mL.	118
Recurrent herpes labialis (RHL) / Herpes simplex labialis (HSL)	Herpesviridae	Docosanol	*Saussurea obvallata*	Saturated 22-carbon aliphatic alcohol	Docosanol targets HSV-1 by inhibiting viral entry into host cells and preventing its replication and the development of drug-resistant mutant viral strains	85, 106, 107, 109, 110, 112, 113, 115, 116

Arctigenin and other lignans

Arctigenin (AR), which occurs naturally in *Saussurea medusa*, was found to have immunomodulatory properties[52]. Two lignans, isolated from *S. medusa* and shown in **Fig. 9**, induced immunosuppressive activity: 2α-Guaicyl-4-oxo-6α-catechyl-3,7-dioxabicyclo[3.3.0]octane **(14)** and 1α-Hydroxy-2α,4α-guaicyl-3,7-dioxabicyclo[3.3.0]octane **(15)**. They were studied for their inhibitory effect on cytokine production. When compared to the standard drug, prednisolone, the investigations revealed a strong inhibitory effect on cytokine generation from LPS (or phytohemagglutinin)-stimulated human peripheral mononuclear cells[66].

Pectin

Pectins are valuable plant-based components that are used in food and pharmaceutical preparations. Immunomodulatory activity is one of the many bioactivities of pectins and their derivatives[120].

Rutin

The nitric oxide (NO), which the inducible nitric oxide synthase (iNOS) produces in huge amounts. Although NO is crucial in the human immune system as a defense mechanism against numerous pathogens, excessive NO production can be harmful and lead to autoimmune disorders, septic shock, and rheumatoid arthritis. As a result, medicinal drugs that suppress iNOS may be effective in treating certain inflammatory diseases. Rutin is a flavonoid that is found in *Saussurea involucrate*. However, when cotreated with an ethyl acetate extract of *S. involucrate* or rutin, the levels of the COX-2 and iNOS bands were significantly decreased when compared to D-gal therapy alone. These findings indicate that ethyl acetate extract of *S. involucrate* or rutin may possess immunospressive properties[124].

Pulchellamin G

Pulchellamin G, an amino acid-sesquiterpene lactone, from *Saussurea pulchella*. Pulchellamin G inhibited the mRNA and protein expression of inducible nitric oxide synthase (iNOS) and iNOS-derived nitric oxide (NO)[125].

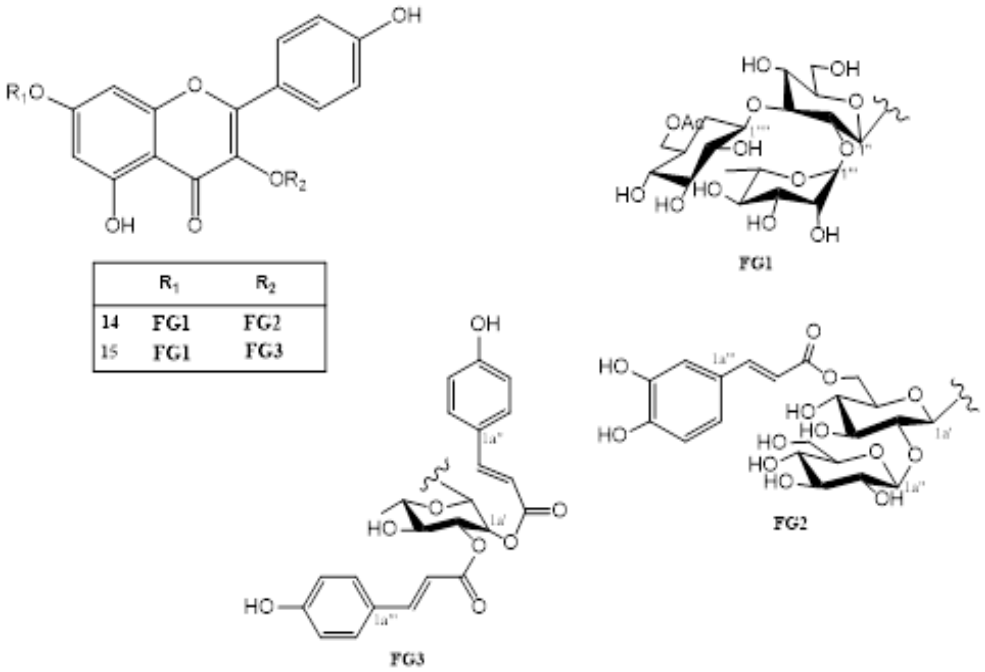


Fig. 9 : Two lignans isolated from *S. medusa* **(14), (15)** induced immunosuppressive activity [66].

Inulin

Inulin, a polyfructose extracted from Saussurea lappa roots, contains 95.89% w/w fructose and has immunostimulant properties, potentiating delayed-type hypersensitivity response to sheep red blood cells (SRBC) and increasing total white blood cell (WBCs) count[22]. The study evaluated inulin intraperitoneal (i.p.) suspension on sheep red blood cell-induced delayed-type hypersensitivity (DTH) reactions in mice. Results showed that inulin may activate T lymphocytes, which release lymphokines and vasoactive amines, which may mediate the hypersensitive response by attracting and stimulating macrophages[126]. It has been found that insoluble antigen-presenting cells (APC) activators like inulin, when incubated with serum, create an enzymatically active complex that can activate C3 and C5 components of the complement system[127]. When given at doses of 100 and 200 mg/kg, the hydroalcoholic extract of *S. lappa* causes a rise in white blood cell count, spleen weight, phagocytic activity, and antibody-secreting cells[128], as well as a reduction in anaphylactic symptoms in animals. Thus, the extract exhibited a dose-dependent humoral as well as a cell-mediated impact. The humoral immune responses are unaltered when this extract is used at low doses (100 mg/kg), but the antibody titer has been observed to be higher at 200 mg/kg[22].

Costunolide, dehydrocostus lactone, and guaianolides of *Saussurea costus*

Higher doses of the hydroalcoholic root extract of *Saussurea costus* (Falc.) Lipsch., as one of the rasayanas, suggested the possibility of immunomodulatory activity in the immune system, both humoral and cellular[128], as shown in **Table 4**. Rasayanas, botanical immunomodulators in Ayurveda, improve mental performance and slow senescence by enhancing the psycho-neuro-immune axis through their effects on histamine release, cytokine production, and cellular receptor expression[129]. Costunolide and dehydrocostus lactone from *Saussurea costus* were found to reduce the cidal activity of cytotoxic T lymphocytes by inhibiting the rise in tyrosine phosphorylation in response to T cell receptor crosslinking at IC_{50} ranging from 3.6/μM to 10/μM in $CD8^+$ CTL clone OE4[97, 130, 131]. Constunolide may benefit in the study of its effect on allergic rhinitis and may be helpful in immunocompromised patients[117]. *Saussurea costus* compounds, including dehydrocostus lactone, mokko lactone, and other guaianolides, were studied for structure-activity. They were found to inhibit CTL killing function and intercellular adhesion molecule-1 (ICAM-1) activation, with guaianolides, which have a α-methylene-γ-lactone moiety, showing significant inhibition[69, 130, 132, 133]. Costunolide also has significant immunological effects in addition to its range of biological effects. In fact, costunolide inhibits carcinogenesis like other sesquiterpene compounds that cause apoptosis in cancer cells[134].

Cynaropicrin and Tannins content of *Saussurea costus*

S. costus has an immunostimulant effect due to the action of cynaropicrin **(16)** shown in **Fig. 10** and tannins content[71, 135, 136] by raising leukocytic count, phagocytosis, and antibody-secreting cells[128], as well as inhibiting reduced glutathione (GSH) oxidation in a dose-dependent manner[135]. Thiols, particularly cysteine and glutathione, are crucial for lymphocyte function and play a vital role in intracellular defense mechanisms against harmful stimuli, including oxidative stress[137], as well as a non-enzymic defensive mechanism against free radicals[138]. In addition, complement inhibitor substances found in *S. costus* are useful in the treatment of disorders like rheumatoid arthritis, respiratory distress, and systemic lupus erythematosus, which are caused by a marked activation of the complement system[65].

Table 4: Immunomodulator agents isolated from *Saussurea* genus plants.

Immunomodulator agent	Source	Chemical class.	Effect/Mechanism	References
Arctiin	Ethyl acetate soluble fraction of dichloromethane : methanol (1:1) extract of *Saussurea heteromalla*	Lignan	Increase immune response.	33, 35
Curcumene	Hexane extract, methylated fraction, SPME extracted oil using GC – MS of Egyptian marketed *Saussurea costus*	Aromatic sesquiterpene	–	121
Arctigenin and other lignans	*Saussurea medusa*	Lignan	Immunomodulatory properties and strong inhibitory effect on cytokine production.	52, 66
Pectin	*Saussurea laniceps*	Polysaccharide	–	120
Rutin	*Saussurea involucrate*	Flavonoid	Immunosuppressant inhibit the production of NO, which is crucial in the human immune system as a defense mechanism against numerous pathogens.	124
Pulchellamin G	*Saussurea pulchella*	amino acid-sesquiterpene lactone	Inhibit the mRNA and protein expression of iNOS and NO.	125
Inulin	Hydroalcoholic extract of *S. lappa* roots	Polysaccharide	Inulin significantly potentiates the delayed-type hypersensitivity response to sheep red blood cells, increasing total WBCs count and activating T lymphocytes.	22, 98, 126
Costunolide , dehydrocostus lactone, mokko lactone, and other guaianolides	Hydroalcoholic extract of *Saussurea costus* Falc. Lipsch. root (Kuth)	Sesquiterpene lactones and Guainolide sesquiterpene	Benefit in allergic rhinitis and immunocompromised patients. Immunomodulatory activity in the immune system, both humoral and cellular by preventing the elevation in tyrosine phosphorylation in response to T-cell receptor cross-linking. Costunolide inhibited the killing activity of CTL through preventing the increase in Tyrosine phosphorylation in response to the cross linking of T cell receptor. Dehydrocostus possessing an α-methylene-γ—lactone moiety exhibited significant inhibitory activity towards the killing function of CTL and the induction of ICAM-1.	117 165 69, 130, 132, 133

Table 4: Continued.

Guaianolides	*Saussurea costus* root	Sesquiterpene lactones	–	117
Cynaropicrin & Tannins	*S. costus*	Sesquiterpene lactone & polyphenolic biomolecules	They have immunostimulant effects by raising leukocyte count, phagocytosis, antibody-secreting cells, and inhibiting reduced glutathione oxidation in a dose-dependent manner.	71, 135, 137
Cynaropicrin	Hydroalcoholic extract of *Saussurea costus* Falc. Lipsch. Root (Kuth)	Sesquiterpene lactone	Immune-suppression effects on the release of cytokine, and nitric oxide production.	165, 139-143
Flavones content & Ethanolic extract of *S. involucrata*	*S. involucrata*	Flavones content: Flavonoids	–	23
Sesquiterpenes & Flavonoids	*S. laniceps*	Sesquiterpene lactone & Flavonoids	–	21
Scopoletin	*S. laniceps*	Hydroxycoumarin	It has anti-oxidant and immunomodulatory properties due to its aromatic hydroxyl group.	21, 156, 157
S. lappa ethanolic extract	*Saussurea lappa*	–	–	158, 159, 160, 161, 162, 163, 164

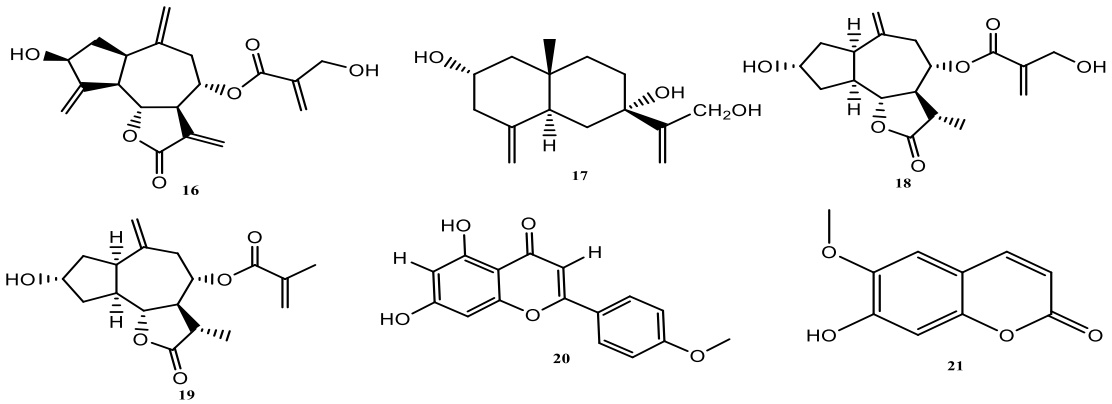


Fig.10: Immunomodulatory agents from *Saussurea* genus: Cynaropicrin **(16)** is a guaianolide-type sesquiterpene lactone has immunomodulatory properties[136].
3α,7α,12-Trihydroxyeudesm-4(15),-11(13)-diene **(17),** 3α,8α -Dihydroxy-1α H,5α H,6β H,7α H,11β H-guai-4(15),10(14)-dien-6,12-olide 8-O -2-hydroxymethylacrylate **(18),** 3α,8α -Dihydroxy-1α H,5α H,6β H,7α H,11β H-guai-4(15),10(14)-dien-6,12-olide 8-O -(2-methyl)acrylate **(19)** are three sesquiterpenes from *S. laniceps* showed immunosuppressive activity[66].
Acacetin **(20)**[23] and Scopololetin **(21)**[157] from *S. laniceps* showed immunomodulatory properties.

Cynaropicrin

Cynaropicrin inhibits the proliferation of leukocyte cancer cell lines like U937, Eol-1, and Jurkat T cells in a dose-dependent mannar. IC_{50} values were 10.90, 2.36, and 3.11μmol/l, respectively[139]; however, change liver cells and human fibroblast cell lines do not respond strongly to cynaropicrin[97, 140]. Cynaropicrin, found in *S. costus*, is an immunomodulator that helps treat conditions like systemic lupus erythematosus, rheumatoid arthritis, and respiratory discomfort by inhibiting cytokine release[71]. Cynaropicrin significantly suppressed CD4+, CD8+ T- and B-lymphocytes proliferation in treated cells with concanavalin A, lipopolysaccharide, phytohemagglutinin, and interleukin-2. Its inhibition is due to a chemical reaction with the SH group of l-

cysteine, which attacks target proteins, causing irreversible covalent binding[141]. Cyanopicrin has immunosuppressive and immunomodulatory effects on the release of cytokinase[142].

Cynaropicrin is a sesquiterpene lactone with a 5-7-5 fused tricyclic skeleton and six stereocenters. Its crucial pharmacophore is the g-butyrolactone ring. Cynaropicrin has also been reported from these botanical sources: the aerial parts of *S. salicifolia*, *S. eopygmaea*, *S. calcicola*, the aerial parts of *S. pulchella*, *S. lappa*, *S. salsa* (Pall.) Spreng., *S. amara*, *S. katochaete*, the aerial parts of *S. amurensis*, the aerial parts of *S. lipshitzii*, *S. alata*, and *S. affinis*. It has strong antiviral activity against all HCV genotypes, with EC_{50} values at low micromolar levels. It inhibits the HCV lifecycle at its early stages, including cell-free and cell-cell infection. Cynaropicrin suppresses HCV genotypes 1a, 1b, 2b, 3a, 4a, 5a, 6a, and 7a, demonstrating pan-genotypic antiviral action. This makes it an attractive choice for developing novel and inexpensive pan-genotypic entry inhibitors of HCV infection as well as treating CD29- and CD98-mediated disorders like virus-induced chronic inflammation and leukocyte cancer cell invasion[143].

Ethanolic extract and flavones content of *S. involucrate*

Specific components of *S. involucrata*, such as flavones[144, 145], as well as ethanolic extract[146], have been found to modulate immunity[23]. *S. involucrata* suppressed non-specific defense mechanisms and delayed hypersensitivity in mice, but it boosted humoral immune activity when greater dosages of *S. involucrata* were given[146]. Furthermore, considerable improvements in mouse immunological function were seen, as evidenced by higher percentages of lymphocyte transformation caused by PHA, serum hemagglutinin antibody titers against SRBC, and hemolysin antibody titers[144]. Apart from that, *S. involucrata* injection of the same concentration stimulated T lymphocyte proliferation while inhibiting B lymphocyte proliferation[147], which serves as the ultimate proof of *S. involucrata*'s performance in the two-way adjustment function. *S. involucrata*, known for its revitalizing powers, preserves body equilibrium in traditional Chinese medicine. Its ethanolic extract of *S. involucrate* flower (Sau) lowers iNOS protein/mRNA levels in brain tissue in the severe acute pancreatitis (SAP) group, suggesting its potential as an anti-iNOS treatment[148].

Sesquiterpenes and Flavonoids

The immunomodulatory and antioxidant potencies of *S. laniceps* have been demonstrated to be strongly connected with activities on antiaging and antifatigue as well as promotion of immune function, contributing to the diverse therapeutic effects of the herb[149, 150]. Previous studies have demonstrated that three sesquiterpenes from *S. laniceps* 3α,7α,12-Trihydroxyeudesm-4(15),-11(13)-diene **(17),** 3α,8α -Dihydroxy-1α H,5α H,6β H,7α H,11β H-guai-4(15),10(14)-dien-6,12-olide 8-O -2-hydroxymethylacrylate **(18),** and 3α,8α -Dihydroxy-1α H,5α H,6β H,7α H,11β H-guai-4(15),10(14)-dien-6,12-olide 8-O -(2-methyl)acrylate **(19)** in **Fig. 10** have inhibitory effects on the proliferation of murine T and/or B cells. For a very long period, *S. laniceps* has been used in Tibetan medicine to treat rheumatoid arthritis, which the prospective immunosuppressive activity supports[66, 151]. *In vitro* and *in vivo* studies found that sesquiterpenes like cynaropicrin and flavonoids like acacetin **(20)**, which are shown in **Fig. 10**, have immunomodulatory effects on murine cell models. Aligning with traditional Chinese medical theory that energizes both the "Yin" and "Yang" essences while maintaining dynamic body balance[152]. This ties in with the traditional idea that *S. laniceps*, as one of the main ingredients in snow lotus medicine, helps to strengthen the body and protect it from a variety of ailments[23]. Cynaropicrin's immunomodulatory effects on cytokine release, nitric oxide generation, and immune suppression in murine macrophages were studied using a herbal formulation (KM1608) as an ingredient[69, 153-155].

Scopoletin

Scopololetin **(21)** in **Fig. 10**, as a coumarin compound that exists in *Saussurea laniceps*, demonstrated exceptional antioxidant efficacy due to its aromatic hydroxyl group[156]. A recent study found compounds with hydroxyl groups have high antioxidant activity, while

those without such a functional group lack reducing power. Scopoletin, with its anti-oxidant and immunomodulatory properties, also has hepatoprotective effects[157].

S. lappa ethanolic extract

The study by Abd El-Rahman investigates the potential benefits of *Saussurea lappa* ethanolic extract in preventing oxidative damage caused by triamcinolone acetonide (TA), a widely used glucocorticoid. Results showed that TA exposure increased leukocytosis, decreased interleukin-12, C-reactive protein, immunoglobulins, and tumor necrosis factor ex, and inhibited oxidative and apoptotic effects. *S. lappa*'s anti-inflammatory, anti-apoptotic, and antioxidant properties make it a potential natural antioxidant to prevent glucocorticoids' negative side effects[158]. The GC-MS analysis of *S. lappa* extract reveals its immunostimulant activity, attributed to various bioactive chemicals like dehydrocostus lactone, costunolide, dihydrodehydrocostus lactone, caryophyllene oxide, saussurea lactone, and beta-costol[159]. Mahmoud Ashry's study found *S. costus* extract has immunomodulatory effects, potentially reducing OXP-induced inflammation and serum TNF-α and IL-1β in rats when combined with Oxaloplatin®. Septilin, an herbal preparation containing *S. lappa*, enhances immune responses in mice[160, 161]. Milad et al.'s study found that dexamethasone injection caused immunosuppression in rats, reducing TLC, C3, C4, and IFNγ, atrophy of the spleen's white pulp, and weak Ki-67 expression. However, administration of *M. oleifera*, *Z. Spina-Christi*, and *S. costus* plant extracts at 200 mg/kg b.wt enhanced immunity at day 28. The combined plant extract showed a higher immune response at 100 mg/kg, presenting no risk to the liver or kidneys[162]. Sesquiterpene lactones from *S. lappa* effectively reduce proinflammatory cytokine TNF-α release and NO overproduction in macrophages. These lactones show effectiveness in managing inflammatory diseases and potentially offer immunospressive effects[163]. Sesquiterpenes with α-methylene-γ-butyrolactone moiety decrease NO production in LPS-activated macrophages, while amino acid-sesquiterpene conjugates, saussureamines A and B, induce HSP 72 and inhibit NF-κB activation and iNOS induction[164]. Santamarin, a sesquiterpene lactone isolated from *Saussurea lappa*, inhibited inducible nitric oxide synthase (iNOS) protein and reduced iNOS-derived nitric oxide (NO)[70].

Conclusion

Asteraceae family is consider one of the most important families in the complementary and alternative medicine. Since ancient times, plants in this family have been used to treat many diseases due to their biological activites. Accordingly, these plants, which are in *Saussurea* genus, acquired high economic value. In this review, we investigated the literature about the plants of *Saussurea* genus and their biological applications, such as their antiviral activity and immunomodulator effects. We found that many plants have antiviral action, including *Saussurea heteromalla*, *Saussurea auriculata, Saussurea obvollata*, *Saussurea medusa, Saussurea namikawae*, *Saussurea laniceps, and Saussurea costus.* These medicinal plants of *Saussurea* genus exhibited antiviral action against several viruses from different families, such as Orthomyxoviridae, Rhabdoviridae, Paramyxoviridae, Flaviviridae, Coronaviridae, Retroviridae, Hepadnaviridae, and Herpesviridae. The findings found that *Saussurea heteromalla*, *Saussurea auriculata*, and *Saussurea obvollata* exhibited antiviral action against enveloped, negative-sense, single-stranded RNA viruses like influenza virus, spring viraemia of carp virus (SVCV), infectious hematopoietic necrosis virus (IHNV), and ranikhet disease virus. On the other side, *Saussurea medusa, Saussurea namikawae, Saussurea obvollata, Saussurea laniceps, and Saussurea costus have been* demonstrated as antiviral drugs against enveloped, positive-sense, single-stranded RNA viruses such as Japanese encephalitis virus (JEV), hepatitis C virus (HCV), SARS-CoV-2 (COVID-19), human immunodeficiency virus type-1 (HIV-1), and other retroviruses. Some plants exhibited antiviral effects against enveloped, double-stranded DNA viruses like the HBV and herpes simplex virus (HSV). We also found that the scientific papers indicated many immunomodulator agents that were isolated from different *Saussurea* species. The experiments revealed that arctiin, curcumene, arctigenin, pectin, rutin, pulchellamin G, inulin,

costunolide, dehydrocostus lactone, cynaropicrin, tannins, acacetin, scopoletin, mokko lactone, and other guaianolides have immunomodulation effects. All of these results confirm the importance of *Saussurea* species as a possible source of effective antiviral drugs and potent medications for the immune system. These species may also be beneficial in future pandemics caused by viruses as a primitive and complementary solution to managing the disease. Furthermore, some of these plants require more experiments and investigations to clearly exhibit their antiviral action and to discover more *Saussurea* species that probably have antiviral or immunomodulatory activities.

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الأنشطة المضادة للفيروسات والمُعدِّلة للمناعة لجنس السوسوريا (العائلة النجمية): بحث مرجعي

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تلعب العائلة النجمية (المُرَكَّبَة) دورًا حاسمًا في الطب التكميلي والطب البديل، حيث تُعرف نباتاتها بتطبيقاتها البيولوجية وقيمتها الاقتصادية العالية. منذ العصور القديمة، تم استخدام هذه النباتات، مثل تلك الموجودة في جنس السوسوريا، لعلاج الأمراض المختلفة. وعلى مر العصور، جذبت نباتات جنس السوسوريا الانتباه وذلك بفضل قُدراتها العلاجية وأهمية تطبيقاتها البيولوجية العديدة. لذلك، هذه هي المراجعة الأولى من نوعها التي تهدف إلى إظهار النشاط المضاد للفيروسات والتأثيرات المناعية لنباتات جنس السوسوريا. لقد قمنا بدراسة مجموعة واسعة من المؤلفات عبر أكبر قواعد البيانات العلمية للحصول على المعلومات اللازمة حول نباتات جنس السوسوريا وتطبيقاتها البيولوجية. ولقد وجدنا أن العديد من نباتات جنس السوسوريا لها نشاط مضاد للفيروسات ضد فيروسات مختلفة، بما في ذلك الفيروسات المغلفة ذات الحمض النووي الريبي (RNA) أحادي السلسلة، سواء كانت سلبية أو إيجابية، ولها أيضًا نشاط مضاد للفيروسات ضد الفيروسات المغلفة ذات الحمض النووي (DNA) مزدوج السلسلة. كما وجدنا أيضًا أن الأوراق العلمية أشارت إلى العديد من العناصر المُعدِّلة للمناعة التي تم فصلها من نباتات مختلفة من جنس السوسوريا. تدعم هذه النتائج أهمية نباتات جنس السوسوريا كمصدر محتمل لأدوية الجهاز المناعي وكأدوية فعالة ضد الفيروسات. قد تكون هذه النباتات مفيدة في الأوبئة التي تسببها الفيروسات في المستقبل كوسيلة أولية ومُساعدة فى إدارة الأمراض. تحتاج بعض هذه النباتات إلى مزيد من الفحص والدراسة لإثبات نشاطها المضاد للفيروسات بشكل واضح، بالإضافة إلى اكتشاف المزيد من نباتات جنس السوسوريا التي من المحتمل أن تمتلك خصائص مضادة للفيروسات أو مُعدِّلة للمناعة.