

Approaches to herbal medicine for HIV infection

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SUMMARY

The problem of combating HIV infection is of great importance for the whole world, so the search for new antiviral agents is very relevant. Along with the search for new synthetic drugs, research is being carried out on antiviral substances of plant origin. The review provides general information about HIV infection, summarizes scientific data on the antiviral activity of herbal medicines. The mechanisms of this action of biologically active substances of medicinal plants are considered.

Keywords: HIV infection, antiviral activity, medicinal plants, biologically active substances.

RESUME

The HIV infection is a worldwide public health problem. Therefore, the search for new antiviral drugs is very important. Along with the search of new synthetic drugs surveys of antiviral substances of plant origin are conducted. In the overview data on anti-HIV effective substances from medicinal plants are summarized with attention on their mechanisms of action.

keywords:HIV infection, antiviral activity, medicinal plants, biologically active substances.

INTRODUCTION

One of the urgent problems of modern medicine is the fight against HIV infection, which in a short time has led to illness and death of millions of people. Mankind learned about it in the early 80s of the last century, when American doctors drew attention to the increasing number of cases of young men with pneumocystis pneumonia and Kaposi's sarcoma. The high mortality rate of the diseased was striking - more than 40%. It was also a surprise that the vast majority of affected men were homo- or bisexual.

In 1981, the causative agent of this disease, the human immunodeficiency virus (HIV), was discovered, which belongs to the family of RNA-containing retroviruses (Retroviridae, from lat. retro - reverse). It is HIV that is the cause of HIV infection, which in the terminal stage ends with AIDS. Then the term appeared: AIDS - AIDS (acquired immunodeficiency syndrome) [2].

HIV infection is a slowly progressive anthroponotic disease. The virus infects cells of the immune system that have CD4 receptors on their surface: T-helpers, monocytes, macrophages, Langerhans cells, dendritic cells, microglial cells. As a result, the immune system is suppressed, AIDS develops, the patient's body loses the ability to defend itself against infections and tumors, secondary opportunistic diseases occur that are not typical for people with a normal immune status.

Millions of people in the world are infected with HIV, and every minute there is a new infection with the virus. For our country, this problem, unfortunately, is also relevant. In Russia, according to data for March 2017, 1,103,150 HIV-infected people were registered, and this number continues to grow.

There are two types of HIV: HIV-1 and HIV-2. The first one is ubiquitous. HIV-2 is endemic in West Africa and places migratorily associated with this area. The HIV-1 population is heterogeneous. The main group of HIV-1 strains is called the M group (from the English main - main). In addition to it, there is also a group O (from the English outlier - lying outside) a group N (from the English new - "new"). In group M, several subtypes or clades of HIV-1 were found, designated by Latin letters, starting with A.

Human immunodeficiency viruses circulating in Russia are also characterized by a heterogeneous population. Subtype A has recently received the greatest distribution (93%). Recombinant strains are identified, in particular, the A/B recombinant, in which the gag gene is represented by subtype A, and the env gene is represented by subtype B. The appearance of subtype C in Primorye has been noted [1, 3, 4].

Currently, medicine has more than three dozen synthetic antiretroviral drugs belonging to several classes and acting on various stages of HIV reproduction. These drugs improve the quality of life of infected people and prolong their lives. However, they cannot rid the body of the integrated virus. In addition, they are highly toxic to patients. With the emergence of resistant strains of HIV, these drugs become ineffective. Therefore, the search for new antiviral agents is very relevant. Along with the search for new synthetic drugs, research is being carried out on antiviral substances of plant origin. It is known that biologically active substances (BAS) from medicinal plants have a wide range of pharmacological activity, including antiviral activity [7].

HIV TREATMENT STRATEGY

The HIV suppression strategy is related to the impact on the various stages of its life cycle, which consists of:

1) attachment of the virus to cell receptors (viral protein gp120 interacts with cellular CD4 receptor and CCR5/CXCR4 co-receptors, which are chemokine receptors);

2) membrane fusion as a result of changes in the conformation of HIV surface proteins;

3) the release of viral RNA from the structural proteins of the virus;

4) reverse transcription of viral RNA using the reverse transcriptase enzyme, in the result is a double-stranded DNA copy of the viral genome;

5) DNA migration into the cell nucleus through the nuclear membrane;

6) integration of DNA into the chromosomal DNA of the cell using integrase (formation proviral DNA);

7) transcription of proviral DNA using RNA polymerase;

8) transport of HIV mRNA from the cell nucleus to its cytoplasm;

9) synthesis of viral proteins;

10) transport of viral proteins, their packaging and assembly of new virions;

11) budding from an infected cell and maturation of virions with the help of a protease [2]. Therefore, the targets of the effects of drugs aimed at suppressing the reproduction of HIV are:

- impact on the process of virus penetration into the cell - interaction with the receptor and co-receptor, disruption of fusion with the cell membrane;

- impact on the release of the viral genome from the membranes and on reverse transcription (RNA to DNA);

- impact on c-DNA integration into the cell genome;

- impact on transcription (DNA in RNA);

- impact on translation and protein cleavage;

- impact on the assembly of the virion and the release of viral particles from the cell.

Synthetic antiretroviral drugs available in medicine belong to several classes and act on different stages of HIV reproduction:

1. HIV reverse transcriptase inhibitors (nucleoside analogues).

2. HIV reverse transcriptase inhibitors (non-nucleoside analogues).

3. HIV protease inhibitors.

4. HIV integrase inhibitors.

5. Inhibitors of HIV entry into the cell (fusion inhibitors and chemokine inhibitors receptors).

It is considered effective to use a combination of drugs of different classes, which provides

more complete suppression of virus reproduction. This therapy is called "highly active antiretroviral therapy" (HAART). There is no doubt that the advent of HAART has radically changed the situation in the treatment and prevention of HIV infection, improving the quality of life of infected people and prolonging their lives [5, 6, 10, 15, 28, 57, 63].

However, the complex nature of HIV allows the virus to adapt to the action of chemotherapy drugs, and drug-resistant strains of HIV develop as a result of therapy. Another problem is the high toxicity of drugs that give numerous side effects. HIV-infected patients must take these drugs for life, because, while there are no means capable of ridding the body of an integrated virus.

The course of HIV infection is closely related to the development of opportunistic infections. Especially often there are concomitant herpetic and cytomegalovirus infections.

Therefore, the search for new therapeutic and prophylactic drugs that are less toxic and active against several viruses at the same time remains very relevant. Capable of also attacking virus reservoirs that are currently inaccessible to the penetration of existing means.

Nature has always been the basis for the search for means of fighting infections, and soon after the discovery of the causative agent of HIV infection, studies began on the effect of biologically active substances (BAS) from natural products on the etiological agent of this infection - the "plague of the 20th century". WHO in 1989 called for attention to the possibilities of ethnomedicine and herbal medicine to combat HIV/AIDS [66].

As a result of the above reasons, there is a need to search for new substances, including those of plant origin. They are relatively inexpensive, they have less pronounced toxic effects, and they can participate in the stabilization of the physiological functions of the body [42, 58, 64].

New antiretroviral substances of plant origin can also be used in combination with already used chemotherapeutic agents, which will provide an additive and/or synergistic effect [26].

Therefore, the study of the experience of ethnomedicine in the use of plant substances can lead to the emergence of not only new antiretroviral agents, but also new mechanisms of action on HIV.

ANTI-HIV PLANT SUBSTANCES

Nature always provides sources of medicines against various diseases. The scientific literature contains a large number of reports of medicinal plants with anti-HIV activity. Extracts from them contain various biologically active substances (BAS), possible candidates for the means of combating HIV infection. Several plant compounds with anti-HIV activity have now been identified. These biologically active substances belong to phenolic compounds (among them flavonoids, coumarins, lignans, tannins), alkaloids, essential oils (terpenes and terpenoids), peptides, polysaccharides.

Phenolic compounds

Phenolic compounds are substances of aromatic nature, the most common and characteristic of every plant and even every plant cell. Among them: simple phenols; benzoic acid derivatives (phenolic acids); phenolic alcohols and phenylacetic acids; phenylpropane derivatives (hydroxycinnamic acids and alcohols, coumarins); flavonoids and isoflavonoids; lignans; polymeric phenolic compounds lignin, tannins, melanins. It turned out that many phenolic compounds have anti-HIV activity. Calceolarioside B, one of the phenolic compounds derived from Siebold's ash (*Fraxinus sieboliana* auct.), binds to HIV gp41 protein and thus prevents its adsorption [25]. Polyphenols, in particular proanthocyanides, extracted from the bark of witch hazel virginiana (*Hamamelis virginiana*) markedly inhibited HIV reverse transcriptase [70]. We also inhibited HIV reverse transcriptase of macrocarpals from the leaves of eucalyptus ballus (*Eucalyptus globulus* Labill) [44] and polyphenol mallotojaponin from Japanese mallotus (*Mallotus japonicas* (Thunb)) [43].

Coumarins are widely distributed in plants of the umbellate, rue, legume,

solanaceous, composite, horse-chestnut. They are localized in fruits, roots, bark, flowers, in a smaller amount - in grass and leaves. It has been shown that coumarin suxdorphin, extracted from pine cones of *Lomatium dissectum* (*Lomatium suksdorfii* (Nutt.) Mathias & Copslapse), modifies HIV replication [29]. Coriandrin, a fluoroisocoumarin, extracted from coriander sativus (cilantro, cilantro) (*Coriandrum sativum* L.), after UV irradiation, inhibits the reverse HIV transcriptase [20].

Flavonoids are found in greater or lesser quantities in almost all higher plants. They are localized mainly in leaves, flowers and fruits, less often in stems and underground organs. In plants, most flavonoids are present in the form of glycosides, which are better soluble in cell sap. The spectrum of pharmacological activity of flavonoids is very wide. In particular, they inhibit the replication of viruses. Thus, Japanese scientists have shown that the flavonoid glycyrrhizin, extracted from licorice (*Glycyrrhiza* sp.), has an in vitro inhibitory effect on infectivity and cytopathic activity of HIV [21]. Later, the therapeutic effect of glycyrrhizin in mice was shown [65]. The flavone glycosides hypokylflavon and robustaflavon from sumac sequential (Japanese wax tree) (*Rhus succedanea* L) inhibited the reverse transcription of HIV RNA [34]. A flavonoid quercetin-3-O-(2-galloyl)-L-arabinopyranosyl extracted from *Okamotoanum* maple (*Acer okamotoanum* Nakai.), inhibited HIV integrase [24].

Lignans are special compounds, polyphenols, formed from tyrosine. Are phytoestrogens, natural hormones. Flax, lemongrass and burdock fruits, and sesame seeds have a high content of lignans. A significant amount of lignans is found in cereals such as: rye, barley, wheat, oats, pumpkin seeds, soybeans, broccoli, beans, carrots, citrus fruits and some berries. Lignans have been found to have antiviral, antitumor, immunomodulatory, antibacterial and antifungal properties. It turned out that they also have anti-HIV activity. Lignans, anolignans A and B from *Anogeissus acuminata* Roxb. Ex DC et Perr.) have inhibitory activity against reverse HIV-1 transcriptase [53]. Globoidian A, lignan from *Eucalyptus ballus* (*Eucalyptus globulus* Labill), inhibited HIV integrase [49].

Tannins (tannins) are vegetable high-molecular phenolic compounds, capable of precipitating proteins, alkaloids and having an astringent taste. Already in 1985, it was shown that cornusin and other tannins extracted from different types of dogwood (*Corpus officinalis* Sieb. et Zuss.), have antiviral activity and inhibit the reverse transcription of HIV RNA [23]. Tannin extracted from the pericarp of Japanese camellia (*Camellia japonica*) inhibits HIV protease1 [14]. Caffeic acid, tannin from hyssop officinalis (*Hyssop officinalis* L.), inhibited HIV replication [27]. Tannins phyllamycin B and retrojusticidin B from *Phyllanthus myrtophylla* (*Phyllanthus myrtifolius* Moon) inhibit reverse transcription of HIV RNA [35].

alkaloids

Alkaloids are a large group of natural nitrogen-containing compounds of a basic nature. They often have strong pharmacological effects. Currently, more than 5000 alkaloids have been isolated from plants. The most widely distributed alkaloids among angiosperms. The seeds of poppy, solanaceous, legumes, kutra, madder, ranunculus, loganium, etc. are especially rich in them. Various alkaloids have anti-HIV activity. For example, psychotrans, alkaloids from ipecac (vomit root) (*Cephaelis ipecacuanha* A. Rich) are inhibitors HIV-1 reverse transcriptase [62]. Michellamine B, an alkaloid from *Ancistrocladus corupensis* (*Ancistrocladus korupensis* D. Thomas & Gereau), inhibits HIV-induced cell death and virus replication in various human cell lines as well as in cultures of peripheral blood leukocytes and monocytes. It is active against laboratory and clinical strains of HIV-1 and some strains of HIV-2 [38].

Essential oils

Essential oils of plants are a complex complex of substances in which over

500 individual components. Essential oils are dominated by terpenes and terpenoids. These compounds are found in the free state as esters or glycosides. In addition to terpenes, essential oils contain other substances that have aroma. These are esters of organic acids of the aliphatic series, as well as benzoic, phenylacetic and cinnamic acids, glycosides (vanillin), aldehydes, coumarins, mustard oil, indole, etc. Essential oils are found in various plant organs (flowers, petals, flower buds, fruits, seeds, leaves, bark, wood, roots, rhizomes) and in varying amounts. Terpenes and terpenoids have anti-HIV activity.

Terpenes are unsaturated hydrocarbons. The name "terpene" comes from the word turpentine. - turpentine, which is an essential oil of conifers. Terpenes can be considered as derivatives of isoprene. Maslinic Acid, Ursolic Acid, Japanese Gravity Terpenes (*Geum japonicum* Thunb. G. faueriei Lev.) inhibit the action of HIV pronase [67]. Limonin and nomelin, citrus terpenes (*Citrus* spp.) inhibit HIV replication¹ in infected human mononuclear cells [8].

Terpenoids are oxygen-containing terpenes. Terpenoids outnumber all other substances of secondary origin. About 10 thousand of them are already known. Antiretroviral activity with different mechanisms of action has been studied with some terpenoids. Betulinic and platanoic acids obtained from the leaves of the myrtle tree *syzygia* (*Syzygium claviflorum*) and tested for H 9 lymphocytes inhibited HIV replication [13]. It should be noted that betulinic acid and its derivatives have a wide spectrum of antiviral activity. Further research led to the creation of a compound (with the properties of betulinic acid) obtained from *Syzygium claviflorum*, the drug "bevirimat" (research code MRS- 4326), an inhibitor of HIV maturation [36]. The drug was developed by Panocos and has reached stage IIb clinical trials. It has also been shown that nigranic acid, a terpenoid from *Schisandra sphaerandra* (*Schisandra sphaerandra* Stapf.), inhibits HIV reverse transcriptase¹ [60]. Pentacyclic terpenoids from African *maproupea* (*Maproupea africana* Muell. Arg.) inhibited HIV-1 reverse transcriptase [52]. Actein is a tetracyclic triterpenoid saponin from black cohosh *racemose* (*Cimicifuga racemose*) has a pronounced anti-HIV activity [56]. Escin is a mixture of triterpenoid saponins from the seeds of Chinese horse chestnut (*Aesculus chinensis*) had an inhibitory effect on the activity of HIV-1 protease [68].

Polysaccharides

Polysaccharides are complex high molecular weight carbohydrates that consist of many monosaccharides. They are among the main sources of energy as a result of the body's metabolism. Plant polysaccharides have antibiotic, antidote, antitumor and antiviral activities. Significant anti-HIV activity is shown by high-polymer polyanionic polysaccharides. These compounds are low toxic and may have the adsorption properties of viral particles. Variations in polymer size, the nature of sugar residues, and the distribution of the number of charged groups open up new possibilities in the design of new anti-HIV drugs. For example, it has been shown that polysaccharides extracted from *Rhizophora* leaves (*Rhizophora apiculata*) and the bark of the pointed *Rhizophora* (*Rhizophora mucronata*), protected MT-4 cells from HIV-induced CPP and inhibited the expression of p24 HIV capsid protein, preventing the binding of the virus to the cell and the formation of syncytium [54]. Prunellin is a polysaccharide, a purified extract from the common blackhead (*Prunella vulgaris* L.) inhibited in vitro HIV-1 infection [69]. High molecular weight fractions of polysaccharides extracted from *Thuja occidentalis* (*Thuja occidentalis* L), increased the production of cytokines during HIV infection [45].

Peptides and proteins

Peptides are relatively short protein molecules (30–40 amino acids). Peptides of plant origin have many biological activities. MAP30 derived from Indian *Momordica* (Crazy Cucumber, Bitter Gourd) (*Momordica charantia* Lipp.), GAP31, DAP32. DAP30 obtained from *Gelonium multiflorum* (*Gelonium multiflorum* A. Juss), bind to HIV RNA and cDNA, inactivate ribosomes and inhibit the formation of syncytium,

reverse transcriptase, integrase, and p24 protein expression [19, 30, 31, 32]. TAP 29 from *Trichosanthes kirilovii* (snake cucumber) (*Trichosanthes kirilowii* Maxim.) inhibits reverse transcription HIV RNA [30]. The protein griffithsin (GRFT) binds to HIV glycoproteins and prevents its adsorption to cells. It is derived from tobacco (*Nicotiana benthamiana*), into the cells of which with the help genetically engineered the gene for this red algae proteingrft. According to the authors studies, GRFT is the most potent of all known HIV inhibitors [47].

MECHANISMS OF ACTION OF ANTI-HIV ACTIVITY BAS OF MEDICINAL PLANTS

A large number of articles are devoted to studies of biologically active substances of medicinal plants that inhibit the reverse transcription of HIV RNA and thereby suppress the reproduction of the virus. Attention is drawn to a large range of biologically active substances that cause this effect. When searching for natural inhibitors of HIV reverse transcriptase, it was found that many compounds of various chemical nature have such activity: polyphenols, among them flavonoids (glycyrrhizin, hypokylavon and robustaflavon, eekalein, quercetin, myricetin, baicalin, etc.), coumarins (coriandrin, suxdorphin), lignans (anolignan A and B, phyllamycin B and retrojusticidin B), tannins (caffeic acid, cornusin, etc.), alkaloids (psychotrines, mishellamine B), terpenes (harcisaterpene A, harcisaterpene B, 12-deoxyphorbol-13) and terpenoids (hydroxyma prunic, betylinic, platanic, nigranic acids), peptides (MAP30, MRK29, TAP29) and polysaccharides. The results of these studies are presented in table. one.

Table 1

BAS of plant origin with activity against HIV.
Target - reverse transcriptase

BAS	Connection class	plant name	Link
Hydroxymaprunic acid, hydroxybenzoate	Terpenoids	African mapruna (<i>Maproupea africana</i> Muell. Arg.)	52
betylinic acid, platanoic acid	Terpenoys	<i>Syzygium claviflorum</i> (<i>Syzygium claviflorum</i> (Roxb.)	thirteen
Nitidine	Alkaloid	Asian <i>Todalia</i> (<i>Toddalia asiatica</i> Lam.)	62
Eekalein, quercetin, myricetin, baicalin	Flavonoids	Red oak (<i>Quercetts rubra</i> L.) and others	48, 59, 61
Nigranic acid	Terpenoids	Lemongrass spherical (<i>Schisapdra sphaerapdra</i> Stapf.)	60
Proanthocyanides	Polyphenols	<i>Hamamelis virginiana</i> (<i>Hamamelis virginiana</i>)	eleven
Psychotrins	alkaloids	<i>Ipecac, vomit</i> (<i>Cephaelis irecasualla</i> A. Rich,)	62
Hypokylavone and robustaflavon	Flavonoids	Sumac serial (Japanese wax tree) (<i>Rhus succedanea</i> L)	34
Michellamine B (Michelamipe V)	Alkaloid	<i>Ancistrocladus corupensis</i> (<i>Ancistrocladus korupensis</i> D. Thomas & Gereau)	38
Suksdorfin	Coumarin	<i>Lomatium dissected</i> (<i>Lomatium suksdorfii</i> (Nutt.) Mathias & conslapse)	29

Coriandrin	Coumarin	Coriander, coriander, cilantro 20 (<i>Coriandrum sativum</i> L.)	
Hypericin	Quinone	St. John's wort (<i>Hypericum perforatum</i> L.)	17
Harcisaterpen A, harcisaterpene B	Terpenes	Garcinia is beautiful <i>Garcinia speciosa</i> Wall)	55
12-deoxyphorbol-13(3E, 5E- decadienoate)	Terpene	Agaloch tree (<i>Excoecaria agallocha</i> L.)	eleven
caffeic acid	Tannin	Hyssop officinalis (<i>Hyssop officinalis</i> L.)	27
Kornusin and others.	Tannins	Dogwood officinalis and other species (<i>Corpus officalis</i> Sieb.et Zuss.)	23
Svertifranchised	flavonoid	Svetia Franchiana (<i>Swertia franchetiana</i> H.Smith.)	51
Salaspermic acid	flavonoid	<i>Tripteridium Wilford</i> (<i>Trypterium wilfordii</i> Hook F)	9
Glycyrrhizin	flavonoid	Licorice (<i>Glycyrrhiza</i> sp.)	21, 65
Anolignan A and B	Lignans	Anogenesis pointed (<i>Anogeissus acuminata</i> Roxb. Ex DC et Perr.)	53
Phyllanthin B and retrojusticin B	Lignans	<i>Phyllanthus myrtophyllum</i> (<i>Phyllanthus myrtifolius</i> Moon)	35
Methyl nordi hydroguaiaretic acid	Lignan	A large number of woody plants	sixteen
Corilagin and 1,3,4,6-tetra- O-galloyl- β -D-glucopyranose	Phenolic connections	<i>Hamamelis hyssopifolia</i> (<i>Chamaesyce hyssopifolia</i> (L.) Small)	33
Macrocarpals	Phenolic connections	Eucalyptus ball (<i>Eucalyptus globulus</i> Labil)	44
mallojapanese	Phenolic connections	Mallot Japanese (<i>Mallotus japonicus</i> (Thunb))	43
Repandusinic acid	Phenolic connections	<i>Phyllanthus niruri</i> (<i>Phyllanthus niruri</i> L.)	46
Polysaccharides	Polysaccharides	Thuja western (<i>Thuja occidentalis</i> L.)	45
MAP30 MRK29	Proteins	Momordica, Indian or mad cucumber, bitter gourd (<i>Momordica charantia</i> Linn.)	22, 32
TAP29	Protein	Trichosanthes Kirilova (snake cucumber) (<i>Trichosanthes kirilowii</i> Maxim)	32

In table. Figure 2 presents some results of studies of plant-derived biologically active substances that inhibit the activity of the HIV integrase enzyme involved in the integration of viral c-DNA into the host DNA. The ability to inhibit integrase activity was established for flavonoids (quercetin), terpenoids (curcumin), lignans (globoidian A) and peptides (MAP30, GAP31, DAP32, DAP30).

table 2

BAS of plant origin with activity against HIV.
Target - integrase

BAS	Class connections	plant name	Link
Quercetin-3-O-2galloyl) a-L-arbinopyranosyl	flavonoid	Maple okamotoanum (Acer okamotoanum Nakai.)	24
Quercetin	flavonoid	Oak red (Quercus rubra L.)	12
Globoidian A	Lignan	Eucalyptus ball (Eucalyptus globulus Labil)	49
Curcumin	Terpenoid	Turmeric, Indian saffron (Curcuma lopga L.)	37
MAP30, GAP31, DAP32. DAP30	Proteins	Momordica. Indian or mad cucumber, bitter gourd (Momordica charaptia Lipp.), Gelonium multiflorous (Gelopium multiflorum A.Juss)	19, 30, 31.32

In table. 3 shows the results of some studies of plant-derived biologically active substances with activity against HIV protease. Viral protease carries out the final formation of core proteins and enzymes of the mature virion. This process occurs in the last stages of virus assembly during virion budding from the cell membrane. Unlike reverse transcriptase inhibitors, HIV protease inhibition acts directly on the pool of infected cells, disrupting the production of infectious virions. The identified HIV protease inhibitors are mainly terpenes (limonin, nomelin, butyric acid, ursolic acid, uvaol) and terpenoids (ganoderic and carnosolic acids).

Table 3

BAS of plant origin with activity against HIV.
Target - protease

BAS	Connection class	plant name	Link
Limonin, nomelin	Terpenes	citruses (Citrus spp.)	eight
Ganoderic acid	triterpene	Ganoderma shiny (Ganoderma lucidum (Leyss. ex Fr. Karst.)	39
Butyric acid, ursolic acid	Terpenes	Japanese gravel (Geum japonicum Thunb. G. faueriei Lev.)	67
carnosolic acid	Terpenoid	Rosemary officinalis (Rosmaripus officipalis L.)	50
Ursolic acid, uvaol	Terpenes	Hawthorn pinnatifida (Crataegus pinnatifida Bge.)	40
Escin	Terpenoid saponins	Chinese horse chestnut (Aesculus chinensis)	68

In table. Figure 4 presents some results of research on BAS of plant origin, which have activity that prevents the adsorption of HIV on cells. BAS,

disrupting the interaction of the virion and the target cell should be considered as the most promising means of herbal medicine. Disruption of glycoprotein processing results in the inability of HIV virions to attach to CD4 cellular targets. Calceolarioside B (a component of phenolic acid) binds to the HIV gp41 protein and thus prevents the adsorption of the virus. Mannose-specific lectins block HIV-1 binding to human H9 cells and lymphocytes *in vitro*. Polysaccharides and alkaloids can also interfere with the process HIV adsorption.

Table 4

BAS of plant origin with activity against HIV.
Target - adsorption of the virus

BAS	Connection class	plant name	Link
Calceolarioside B	Phenolic compound	Ash Siebold (<i>Fraxinus sieboliana</i> auct.)	25
Mannose-specific lectins	Lectins	Snowdrop (<i>Galanthus</i> sp.), daffodil (<i>Narcissus</i> sp.), amaryllis (<i>Amaryllis</i> sp.), gerardia (<i>Gerardia</i> sp.)	41
Shumanificin 1	Alkaloid	shumanniphyton magnificent (<i>Schumanniorhutop magpificum</i> (K. Schum.) Narms)	eighteen
Prunellin	Polysaccharide	Chernogolovka ordinary (<i>Rupella vulgaris</i> L.)	69
"Bevirimat"	Terpenoid	Myrtle tree syzygia (<i>Syzigium claviflorum</i>)	36

CONCLUSION

An analysis of the literature shows that many of the world's leading laboratories are engaged in the search for drugs active against HIV. Including, many bioactive substances of plant nature have been studied, in some cases exhibiting pronounced anti-HIV activity *in vitro*. The above data indicate that many plants have anti-HIV activity. BAS plants that determine the antiviral action are phenolic compounds (among them flavonoids, coumarins, lignans, tannins), alkaloids, essential oils (terpenes and terpenoids), peptides, polysaccharides. These biologically active substances act directly on different stages of HIV reproduction, or by activating the immune system. Summing up the data on the anti-HIV activity of various classes of substances of plant origin, it should be noted that most of them have an inhibitory effect on the activity of reverse transcriptase, while BAS of only a few classes show their activity against other HIV enzymes. So far, herbal medicines are not used in the treatment of HIV infection, but scientists are pinning their hopes on several biologically active substances with anti-HIV activity, candidates for preclinical and clinical trials. Further searches for new anti-HIV drugs among natural compounds from plants seem promising.

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