INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com ISSN 2230 – 8407

Review Article

ANTIVIRAL POTENTIAL OF MEDICINAL PLANTS: AN OVERVIEW

Ruwali Pushpa, Rai Nishant, Kumar Navin, Gautam Pankaj*
Department of Biotechnology, Graphic Era University, Clement Town, Dehradun, India
*Corresponding Author Email: gautampankaj76@gmail.com

Article Received on: 18/03/13 Revised on: 01/04/13 Approved for publication: 12/05/13

DOI: 10.7897/2230-8407.04603
IRJP is an official publication of Moksha Publishing House. Website: www.mokshaph.com

ABSTRACT
The term 'Antiviral agents' has been defined in very broad terms as substances other than a virus or virus containing vaccine or specific antibody which can produce either a protective or therapeutic effect to the clear detectable advantage of the virus infected host. The herbal medicine has a long traditional use and the major advantage over other medicines is their wide therapeutic window with rare side effects. There are some disadvantages of synthetic drugs like narrow therapeutic window and more importantly the various adverse side effects which occur quite frequently. Due to these disadvantages and other limitations, there is an increasing trend in the field of research for discovering new and noble drugs based on various herbal formulations. This review attempts to address the importance of developing therapeutic herbal formulations from various medicinal plants using the knowledge based on traditional system of medicines, the Ayurveda. Although natural products have been used by civilization since ancient times, only in recent decades has there been growing research into alternative therapies and the therapeutics use of natural products, especially those derived from plants. Plants synthesize and preserve a variety of biochemical products, many of which are extractable and used for various scientific investigations. Therefore, medicinal plants proved to be a major resort for the treatment of diseases and sicknesses by traditional healers in many societies.
Keywords: antiviral, herbal formulations, Ayurveda, medicinal plants.

INTRODUCTION

Viral diseases are responsible for considerable morbidity and mortality worldwide. Infectious viral diseases are still major threat to public health and remain a major problem all over the world[1]. A number of cases of viral diseases have been reported from different regions of the world including India (Table 1 and Table 2)[2]. Lack of specific treatment for viral diseases and constrained therapeutic efficacy of most drugs have led to a dependence on vaccines as preventive measures[3]. The common treatment for these illnesses includes various drugs but resistant pattern of some pathogenic viruses worsen the scenario and these drugs also have some serious side effects on patients[1]. Nowadays, traditional medicines are revalued through extensive research programs for their therapeutic potential[4]. Medicinal plants have been used in traditional health care systems since prehistoric times and are still the most important health care source for the vast majority of the population around the world. It is estimated that 70-80% of people worldwide rely on traditional herbal medicine to meet their primary health care needs. Globally, millions of people rely on medicinal plants not only for primary health care, but also for income generation and livelihood improvement[5]. In field of traditional medicines, India has a rich cultural heritage comprising of two systems of treatments, i.e. Ayurvedic and Unani systems[6]. Ethno-pharmacological knowledge of traditional herbal medicine usage have been an important source of information and have shown to be very efficient in the identification of bioactive compounds, even when compared to the standard high volume random screening method[7]. Various traditional medicine systems worldwide have herbal formulations as their foundation[8]. Some of them, like that of Tibetan system, remain localized in a country or region, while others, like that of Ayurveda and Chinese systems, gains popularity and are being increasingly used in various parts of the world[9]. For a plant to be called as a medicinal plant it is necessary that its biological activity has been ethanobotanically reported or scientifically established[10]. In Ayurveda system, there are various medicinal plants containing different types of chemical compounds which may acts as a source of various therapeutics agents to cure diseases associated with public health[9]. Although, the field of herbal medicines or we can say the field of Ayurveda has immense opportunities in present day medical sciences and also holds promises for the future as well but it also has its own limitations as all the herbal formulations will ultimately depends on the availability of plants material which directly or indirectly will depend on various factors such as growth cycle of the plant, its local availability and also on the Government restrictions.

Antivirals: A Herbal Approach

Herbal Anti- viral Medicine: An Introduction

The term 'antiviral agents' has been defined in very broad terms as substances other than a virus or virus containing vaccine or specific antibody which can produce either a protective or therapeutic effect to the clear detectable advantage of the virus infected host[6,11]. All over the world, herbal medicines are considered to be one of the most important areas of interest in traditional medicine systems[12]. Man entirely depends on plants and plant products directly for his basic needs as food, clothing and shelter and indirectly for their beneficial influence on climate and maintenance of his immediate and remote environment and this makes plants vital for his survival and the basis of his continued existence. World Health Organization (WHO) has also emphasized, in 1978, on the importance of scientific research into herbal medicine and since then the developing countries of world has started research programs to clinically prove the therapeutic value of their native medicinal plants in order to get them registered as possible addition to the WHO's list of "essential drugs"[13]. In recent times, medicinal plants occupy an important position for being the paramount sources of drug discovery, irrespective of its categorized groups- herb, shrub or tree[14]. Nowadays, the use of traditional medicines for their therapeutic properties is not only restricted to the developing countries.

According to a report published by WHO, nearly 80% of people living in rural areas depends on medicinal plants as primary health care system and their practices solely based on knowledge of traditional use of medicinal plants[14]. According to a FAO report, at least 25% drugs used in modern pharmacopoeia are derived from plant products and many other drugs (synthetic analogues) are being developed on prototype compounds isolated from plants. Drug development programs of pharmaceutical industry have an important role of natural products as more than 50% all modern clinical drugs are originated from natural products[15]. Some of the medicinal plants having antiviral properties against various viruses are reported in various research article (Table 3).

Synthetic Drugs and Their Targets

Many viral infections are still a great danger to humans and often cause death. In the past, deadly viruses caused pandemics in the world. Nowadays, the risk of spreading viruses between continents and countries is even larger. Due to the metabolic properties of viruses, they are difficult to control and there are still relatively few drugs for treatment of viral diseases[16]. For many years viral diseases have been considered as intractable to selective antiviral chemotherapy because the replicative cycle of the virus was assumed to be too closely interwoven with normal cell metabolism so that any attempt to suppress virus reproduction would be doomed to kill (or severely harm) the uninfected cell as well[17]. Synthetic substances for viral infections treatment often proves unsatisfactory and limited due a narrow spectrum of activity, limited therapeutic usefulness, toxicity and resistant viral strains[18]. With the elucidation of virus-specific events as targets for chemotherapeutic attack and the advent of a number of specific antiviral agents, it has become increasingly clear that a selective chemotherapy of virus infections can be achieved and that virus reproduction can be suppressed without deleterious effects on the host. The viral replication cycle can be roughly divided into 10 steps: virus-cell adsorption (binding, attachment), virus-cell fusion (entry, penetration), uncoating (decapsidation), early transcription and early translation, replication of the viral genome, late transcription, late translation, virus assembly, and release. All these steps could be envisaged as targets for chemotherapeutic intervention[17]. Some of synthetic drugs and their respective targets are summarized in Table 4 [19]. The major targets for antiviral formulations are viral envelope and membrane protein. In case of enveloped viruses, the viral envelope is a good target for antiviral chemotherapy because their destruction renders the virus vulnerable to destruction and rendering virus communicability less feasible[11]. The broad-spectrum antivirals target rate limiting events in viral replication cycle such as envelope protein glycosylation, processing and folding or viral-cell membrane fusion during viral uncoating or assembly[20]. Another important target for the design of antiviral formulations had been the viral nucleic acids[11]. The virus specific antivirals target virus-encoded activities (enzymes) like viral polymerase or protease, and these agents usually possess high (100 – 1000) therapeutic indices (TI)[20]. This approach leads to the formation of virus progeny with defective nucleic acids which will be either unstable or give nonsense coding for viral proteins/enzymes, and thus the virulence of the resulting virus can be restrained[11]. However, the drawback of their high specificity is a rapid virus adaptation to the drug and eventual development of drug resistance due to accumulating mutations. The broad-spectrum antivirals are less prone to developing drug resistance but their efficiency is usually a trade-off between some cytotoxicity and anti-viral effects[20]. Nucleoside analogues and other synthetic compounds have traditionally been the primary sources for antiviral agents. The use of antiviral synthetic drugs is often unsatisfactory and limited. Mutant viruses resistant to the existing antiviral agents arise upon treatment or these agents may cause side or toxic effects besides their high costs[3].

Herbal Antiviral Drugs

There is an increasing need for search of new compounds with antiviral activity as the treatment of viral infections with the available antiviral drugs is often unsatisfactory due to the problem of viral resistance coupled with the problem of viral latency and conflicting efficacy in recurrent infection in immune-compromised patients[21]. Investigation for bio-prospecting of natural products can be carried out in two ways. Firstly, the classical method involving phytochemical factors, serendipity and random screening approaches. Second one depends on traditional knowledge and practises or Ethno-pharmacology which provides an alternative approach for the discovery of antiviral agents, namely the study of medicinal plants with a history of traditional use as a potential source of substances with significant pharmacological and biological activities[21,22]. Natural products remain an important source of biologically active substances, especially for the treatment of infectious diseases[1]. Higher plants may serve as promising sources of novel antiviral prototypes[3]. A number of compounds extracted from various species of higher plants have shown antiviral activity. Examples included tannins, flavones, alkaloids, that displayed *in vitro* activity against numerous viruses. Some other examples of classes of antiviral compounds are summarized in Table 5 [23]. It has been suggested that selection of plant on the basis of ethno-medical considerations gives a higher hit rate than screening programmes of general synthetic products[24]. The medicinal use of plants is very old. The writings indicate that therapeutic use of plants is as old as 4000–5000 B.C. and Chinese used first the natural herbal preparations as medicines. In India, however, earliest references of use of plants as medicine appear in Rigveda which is said to be written between 3500–1600 B.C. Later the properties and therapeutic uses of Medicinal plants were studied in detail and recorded empirically by the ancient physicians in Ayurveda (an indigenous system of medicine) which is a basic foundation of ancient medical science in India[25]. Plants have been used as folk remedies and ethno-botanical literature has described the usage of plant extracts, infusions and powders for centuries for diseases now known to be of viral origin[24]. A list summarizing some potential plants having antiviral targets is given in Table 6. Although natural products have been used by civilization since ancient times, only in recent decades has there been growing research into alternative therapies and the therapeutic use of natural products, especially those derived from plants. Herbal preparations are frequently used not only in rural areas in developing countries but also in developed countries in human and veterinary medical practices. As result, a number of studies have been carried out on antiviral activity against several animal and human viruses in all continents[3]. Traditional medicine provides information and represents a reservoir of pharmacologically active substances or drugs. Plants synthesize and preserve a variety of biochemical

products, many of which are extractable and used for various scientific investigations. These phytochemicals that include primary and secondary metabolites have countless benefits to humans, which are exploited as natural pesticides, flavouring, fragrances, medicinal compounds, fibers and beverages. While secondary metabolites have restricted distribution, which is to one plant species or a taxonomically related group of species, primary metabolites are found throughout the plant kingdom. Primary metabolite act as a precursor for bioactive compounds used as therapeutic drugs[21]. The medicinal plants are also rich in essential oils of therapeutic importance[25]. Therefore, medicinal plants proved to be a major resort for the treatment of diseases and sicknesses by traditional healers in many societies[26].

Advantages of herbal drugs

The wide prescription of herbal drugs is mainly due to their effectiveness, less side effects and relatively low cost[27]. Therapeutic uses of medicinal plants in various ailments also have an additional important advantage of their easy availability and thus the traditional medical practitioners widely use medicinal plants in their day to day practice. According to a survey (1993) of World Health Organization (WHO), the practitioners of traditional system of medicine treat about 80% of patients in India, 85% in Burma and 90% in Bangladesh. The Indian medicinal plants used in the traditional systems of medicine proves to be useful in successful management of various disease conditions like bronchial asthma, chronic fever, cold, cough, malaria, dysentery, convulsions, diabetes, diarrhea, arthritis, emetic syndrome, skin diseases, insect bite and also in treating gastric, hepatic, cardiovascular & immunological disorders[25].

Cytotoxicity of Antiviral Phytochemicals

Cytotoxic evaluation is very important and integral part of research involving discoveries of new and potent antiviral drugs. A novel formulation with potent antiviral activity have to be proven as not having any toxicity effects and cytotoxicity assays in a suitable cell culture system are only a part of primary step in this direction. For the purpose of testing, different plants active principals have to be extracted with suitable solvents. The list of commonly used solvents for extraction purpose is summarized in Table 7. Treating cells with these phytochemicals can result in a variety of cell fates. The cells may undergo necrosis, in which they lose membrane integrity and die rapidly as a result of cell lysis. The cells can stop actively growing and dividing (a decrease in cell viability), or the cells can activate a genetic program of controlled cell death (apoptosis). Cells undergoing necrosis typically exhibit rapid swelling, lose membrane integrity, shut down metabolism and release their contents into the environment. Cells that undergo rapid necrosis *in vitro* do not have sufficient time or energy to activate apoptotic machinery and will not express apoptotic markers[29]. Apoptosis is characterized by well defined cytological and molecular events including a change in the refractive index of the cell, cytoplasmic shrinkage, nuclear condensation and cleavage of DNA into regularly sized fragments[20]. Cells in culture that are undergoing apoptosis eventually undergo secondary necrosis. They will shut down metabolism, lose membrane integrity and lyse[30,31]. In past years, a number of methods have been developed to study cell viability and proliferation in cell culture. Colorimetric and luminescence based assays allow samples to be measured directly in the plate by using a micro-titer plate reader or ELISA plate reader. Cytotoxicity assays have been developed which use different parameters associated with cell death and proliferation[32]. Assessing cell membrane integrity is one of the most common ways to measure cell viability and cytotoxic effects. Compounds that have cytotoxic effects often compromise cell membrane integrity. Vital dyes, such as trypan blue or propidium iodide are normally excluded from the inside of healthy cells; however, if the cell membrane has been compromised, they freely cross the membrane and stain intracellular components[31]. Alternatively, membrane integrity can be assessed by monitoring the passage of substances that are normally sequestered inside cells to the outside. One commonly measured molecule is lactate dehydrogenase (LDH)[33]. Lactate dehydrogenase (LDH) is a stable cytoplasmic enzyme present in all cells. It is rapidly released into the cell culture supernatant upon damage of the plasma membrane. The LDH activity is determined in an enzymatic test. The first step is the reduction of NAD^+ to $NADH/H^+$ by the LDH catalyzed conversion of lactate to pyruvate. In a second step, the catalyst (diaphorase) transfers H/H^+ from $NADH/H^+$ to the tetrazolium salt 2-(4-iodophenyl)-3-(4-nitrophenyl)-5-phenyltetrazolium chloride (INT), which is reduced to a red formazan[32]. Protease biomarkers have been identified that allow researchers to measure relative numbers of live and dead cells within the same cell population. The live-cell protease is only active in cells that have a healthy cell membrane and loses activity once the cell is compromised and the protease is exposed to the external environment. The dead-cell protease cannot cross the cell membrane and can only be measured in culture media after cells have lost their membrane integrity[34]. Cytotoxicity can also be monitored using the MTT or MTS assay. This assay measures the reducing potential of the cell using a colorimetric reaction. Viable cells will reduce the MTS reagent to a colored formazan product. Tetrazolium salts are reduced only by metabolically active cells. Thus, 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) can be reduced to a blue colored formazan[32]. A similar redox-based assay has also been developed using the fluorescent dye, resazurin. In addition to using dyes to indicate the redox potential of cells in order to monitor their viability, researchers have developed assays that use ATP content as a marker of viability[31]. Adenosine triphosphate (ATP) that is present in all metabolically active cells can be determined in a bioluminescent measurement. The bioluminescent method utilizes an enzyme, luciferase, which catalyses the formation of light from ATP and luciferin. The emitted light intensity is linearly related to the ATP concentration[32]. Neutral red (3-amino-*m*-dimethylamino-2-methylphenazine hydrochloride) has been used previously for the identification of vital cells in cultures. This assay quantifies the number of viable, uninjured cells after their exposure to toxicants; it is based on the uptake and subsequent lysosomal accumulation of the supravital dye, neutral red. Quantification of the dye extracted from the cells has been shown to be linear with cell numbers, both by direct cell counts and by protein determinations of cell populations[32]. A label-free approach to follow the cytotoxic response of adherent animal cells in real-time is based on electric impedance measurements when the cells are grown on gold-film electrodes. This technology is referred to as electric cell-substrate impedance sensing (ECIS). Label-free real-time techniques provide the kinetics of the cytotoxic response rather than just a snapshot like many colorimetric endpoint assays.

Table 1: Number of cases of some viral diseases in Uttarakhand State and neighbouring states in year 2010

State/UT	No. of Cases					
	Dengue	Rabies	Chikungunya Fever	Viral Hepatitis	Japanese Encephalitis	Acute Respiratory Infection
Uttarakhand	21	03	-----	6645	07	132998
Uttar Pradesh	960	00	05	1977	3540	817467
Delhi	6259	14	120	6510	00	249463
Bihar	287	NR	-----	NR	50	NR
Himachal Pradesh	-----	00	-----	2566	-----	1364166
Madhya Pradesh	174	01	48	5168	-----	578177
Haryana	1082	00	01	1500	01	983342

Table 2: Number of cases of some viral diseases in World (region wise) in the year 2010[2]

Region	No. of Cases				
	Rubella	Yellow Fever	Measles	Mumps	Congenital rubella syndrome
African	2754	714	186675	-----	-----
American	12	23	208	24608	00
South East Asia	-----	-----	50265	-----	-----
European	10551	00	30625	27013	02
Eastern Mediterranean	1398	-----	10072	-----	-----
Western Pacific	45966	-----	49460	486449	-----

Table 3: List of plants showing antiviral properties against various viruses

Virus Name	Plant with anti viral properties	Ref
Herpes Simplex Virus	*Carissa edulis* (*Apocynaceae)*	36
	Phyllanthus urinaria (*Euphorbiaceae*)	8
	Caesalpinia pulcherrima (*Fabaceae*)	8
	Adansonia digitata (*Malvaceae*)	8
	Echinacea (Asteraceae)	10
	Camellia sinensis (Theaceae)	12
	Cissus quadrangularis (Vitaceae)	45
	Ardisia squamulosa (Myrsinaceae)	43
	Artimisai princeps var.orientalis	43
	Astilbe rivularis (Saxifragaceae)	43
	Bergenia ciliate (Saxifragaceae)	43
	Boussingaultia gracilis var pseudobaselloides	43
	Cassiope fastigiata	43
	Centella asiatica	43
	Holoptelia integrefolia (Ulmaceae)	43
	Malclura cochinchinensis (Moraceae)	43
	Mangifera indica (Anacardiaceae)	43
	Nerium indicum (Apocynaceae)	43
	Serissa japonica (Rubiaceae)	43
	Thymus linearis (Lamiaceae)	43
	Allium sativum (Liliaceae)	45
	Swertia chirata (Gentianaceae)	45
	Ocimum basilicum (Lamiaceae)	45
	Solanum nigrum (Solanaceae)	45
Herpes Simplex Virus I	*Hypericum neurocalycinum* (Clusiaceae)	41
	Hypericum salsugineum (Clusiaceae)	41
	Hypericum kotschyanum (Clusiaceae)	41
	Rheum officinale (Polygonaceae)	41
	Aloe barbadensis (Liliaceae)	41
	Rhamnus frangula (Rhamnaceae)	41
	Rhamnus purshianus (Rhamnaceae)	41
	Cassia angustifolia (Caesalpinaceae)	41
	Aglaia odorata (Meliaceae)	43
	Astragalus membranaceus or Radix astragali	43
	Agrimonia pilosa (Rosaceae)	43
	Elytranthe maingayi	43
	Elytranthe globosa (Loranthaceae)	43
	Elytranthe tubaeflora	43
	Eucommia ulmoides (Eucommiaceae)	43
	Melastoma malabathricum (Melastomataceae)	43
	Moringa oleifera (Moringaceae)	43
	Piper aduncum (Piperaceae)	4
	Pithecellobium clypearia (Fabaceae)	43
	Punica granatum (Lythraceae)	43
	Scurulla ferruginea	43
	Ventilago denticulate (Rhamnaceae)	43
Human simplex virus type 2	*Withania somnifera* (Solanaceae)	45
Adenovirus	*Caesalpinia pulcherrima* (*Fabaceae)*	8
	Camellia sinensis (Theaceae)	12

	Artimisai princeps var.orientalis	43
	Ardisia squamulosa (Myrsinaceae)	43
	Boussingaultia gracilis var pseudobaselloides	43
	Serissa japonica (Rubiaceae)	43
	Ocimum basilicum (Lamiaceae)	43
Human Adenovirus Type 1	Black Soyabean extract	8
Influenza Virus	*Geranium sanguineam* (*Geraniaceae*)	8
	Camellia sinensis (*Theaceae*)	8
	Cistus incanus (Cistaceae)	8
	Punica granatum (Punicaceae)	8
	Echinacea (Asteraceae)	8
	Elderberry extract	8
	Cistus incanus (Cistaceae)	9
	Camellia sinensis (Theaceae)	12
	Allium oreoprasum (Alliaceae)	43
	Androsace strigilosa (Saxifragaceae)	43
	Asparagus filicinus (Asparagaceae)	43
	Bergenia ligulata (Saxifragaceae)	43
	Chaenomeles sinensis (Rosaceae)	43
	Myrica rubra (Myricaceae)	43
	Nerium indicum (Apocynaceae)	43
	Verbascum Thapsus (Scrophulariaceae)	43
	Emblica officinalis (Euphorbiaceae)	45
Influenza A and B virus	*Camellia sinensis* (Theaceae)	9
Influenza A (H3N2) and (H1N1) viruses	*Prunus mume* (Rosaceae)	43
Influenza A (H3N2) and B viruses	*Scutellaria baicalensis* (Lamiaceae)	43
Influenza A (H3N2) virus	*Elsholtzia rugulosa* (Lamiaceae)	43
	Hypericum japonicum (Hypericaceae)	43
H1N1,H9N2,H5N1	*Andrographis paniculata* (Acanthaceae)	45
H1N1,H6N1	*Curcuma longa* (Zingiberaceae)	45
H3N2,H1N1	*Sambucus nigra* (Adoxaceae)	45
Avian, Human and Equine strains of influenza A virus	*Geranium sanguineum* (Geraniaceae)	9
Parainfluenza virus type 3,Vaccinia virus, Vesicular stomatitis virus and Human rhinovirus type 3	*Allium sativum* (Liliaceae)	45
Hepatitis B Virus	*Boehmeria nivea* (Urticaceae)	8
	Polygonum cuspidatum (Polygonaceae)	8
	Picrorhiza kurroa (Scrophulariaceae)	45
	Ocimum basilicum (Lamiaceae)	45
Hepatitis C Virus	*Saxifraga melanocentra* (Saxifragaceae)	8
Polio virus	*Guazuma ulmifolia* (Sterculiaceae)	8
	Stryphnodendron adstringens	8
	Elytranthe maingayi	43
	Elytranthe globosa (Loranthaceae)	43
	Elytranthe tubaeflora	43
	Melastoma malabathricum (Melastomataceae)	43
	Piper aduncum (Piperaceae)	43
	Scurulla ferruginea	43
Polio virus type 3, Vaccinia virus, New castle disease virus	*Ocimum sanctum* (Lamiaceae)	45
Viral Haemorrhagic Septicaemia Virus	*Olea europaea* (oleaceae)	8
Severe Acute Respiratory Syndrome-Associated Coronavirus	*Lycoris radiate* (Amaryllidaceae)	8
Vesicular Stomatitis Virus	*Trichilia glabra* (Meliaceae)	8
Corona viruses	*Echinacea* (Asteraceae)	10
Rhinoviruses	*Echinacea* (Asteraceae)	10
Coxsackie viruses	*Echinacea* (Asteraceae)	10
Coxsackie virus B3	*Ardisia chinensis* (Myrsinaceae)	43
	Plumbago zeylanica (Plumbaginaceae)	45
Dengue virus	*Andrographis paniculata* (Acanthaceae)	38
	Momordica charantia (Cucurbitaceae)	38
	Kaempferia parviflora (Zingiberaceae)	43
	Stemona tuberose (Stemonaceae)	43
Dengue Virus type 2	*Azadirachta indica* (Meliaceae)	8
Bovine corona virus and Bovine rotavirus	*Camellia sinensis* (Theaceae)	12
Rotavirus, Cytomegalovirus	*Astragalus membranaceus or Radix astragali*	43
Cytomegalovirus B1	*Bupleurum kaoi*	43
Epstein - barr virus	*Camellia sinensis* (Theaceae)	12
	Boesenbergia pandurata (Zingiberaceae)	43
	Citrus hystrix (Rutaceae)	43
	Languas galanga or Alpinia galangal (Zingiberaceae)	43
Respiratory syncytial virus	*Echinacea* (Asteraceae)	10
	Blumea laciniata (Asteraceae)	43
	Elephantopus scaber (Asteraceae)	43
	Laggera pterodonta (Asteraceae)	43
	Mussaenda pubescens (Rubiaceae)	43
	Schefflera octophylla (Araliaceae)	43
	Scutellaria indica (Labiatae)	43
	Selaginella sinensis (Selaginellaceae)	43
Enteroviruses	*Ocimum basilicum* (Lamiaceae)	43

	Salvia miltiorrhiza (Lamiaceae)	43
Human Immunodeficiency Virus	*Phyllanthus amarus* (Euphorbiaceae)	8
	Zingiber officinale (Zingiberaceae)	45
Human immunodeficiency virus type 1	*Camellia sinensis* (Theaceae)	12
	Ecklonia cava	43
	Prunella vulgaris (Lamiaceae)	43
	Calotropis gigantea (Apocynaceae)	44
	Barringtonia asiatica (Lecythidaceae)	44
	Adransonia digitata (Bombacaceae)	44
	Scaevola sericea (Goodeniaceae)	44
	Pluchea indica (Asteraceae)	44
	Ipomoea congesta (Convolvulaceae)	44
	Cuscuta sandwichiana (Cuscutaceae)	44
	Aleurites moluccana (Euphorbiaceae)	44
	Clermontia aborescens (Campanulaceae)	44
	Ficus prolix	44
	Eugenia malaccensis (Myrtaceae)	44
	Piper methysticum (Piperaceae)	44
	Rhaphiolepsis indica (Rosaceae)	44
	Morinda citrofolia (Rubiaceae)	44
	Psychotria hawaiiensis (Rubiaceae)	44
	Solanum niger (Solanaceae)	44
	Pipturus albidus	44
HIV 1 proviral DNA	*Ocimum gratissimum* (Lamiaceae)	45
Denovirus	*Ocimum basilicum* (Lamiaceae)	45

Table 4: Synthetic Drugs and Their Respective Targets[19]

Drug	Viruses	Chemical Type	Target
Vidarabine	Herpesviruses	Nucleoside analogue	Virus polymerase
Acyclovir	Herpes simplex (HSV)	Nucleoside analogue	Virus polymerase
Gancyclovir and Valcyte ™ (valganciclovir)	Cytomegalovirus (CMV)	Nucleoside analogue	Virus polymerase (needs virus UL98 kinase for activation)
Nucleoside-analog reverse transcriptase inhibitors (NRTI): AZT (Zidovudine), ddI (Didanosine), ddC (Zalcitabine), d4T (Stavudine), 3TC (Lamivudine)	Retroviruses (HIV)	Nucleoside analogue	Reverse transcriptase
Non-nucleoside reverse transcriptase inhibitors (NNRTI): Nevirapine, Delavirdine	Retroviruses (HIV)	Nucleoside analogue	Reverse transcriptase
Protease Inhibitors: Saquinavir, Ritonavir, Indinavir, Nelfinavir	HIV	Peptide analogue	HIV protease
Ribavirin	Broad spectrum: HCV, HSV, measles, mumps, Lassa fever	Triazole carboxamide	RNA mutagen
Amantadine / Rimantadine	Influenza A strains	Tricyclic amine	Matrix protein / haemagglutinin
Relenza and Tamiflu	Influenza strains A and B	Neuraminic acid mimetic	Neuraminidase Inhibitor
Pleconaril	Picornaviruses	Small cyclic	Blocks attachment and uncoating
Interferons	Hepatitis B and C	Protein	Cell defence proteins activated

Table 5: Major classes of anti-viral compounds from plants[23]

Compound	Activity/Target
Terpenoids	
Agastanol & Agastaquinone	Protease
Uvaol & Ursolic Acid	Protease
Garciosaterpene A, C	Reverse transcriptase; Inhibition in syncytium
Vaticinone	Inhibited replication
Betulinic Acid	Inhibited maturation
Glycyrrhizin	Inhibited infectivity, cytopathic activity, replication
Flavonoids	
Baicalin	Reverse transcriptase Infection/entry, replication
Taxifolin (dihydroquercetin)	Inhibited cytopathic activity
Epigallocatechin-3-gallate	Reverse trancriptase
Flavonoid glucuronide	Integrase
Biflavonoids (Ginkgetin)	Influenza virus sialidase
Tetrahydroxyflavone	Influenza virus sialidase
Coumarins	
Calanolide A	Reverse transcriptase
Polyphenols	
Polyphenolic complex	Influenza virus
Alkaloids	
Thalimonine	Influenza virus replication
Indole alkaloid	Influenza virus replication
Lignans	
Rhinacanthin E, F	Influenza virus

Table 6: Antiviral targets of plant species against various viruses

Viruses	Potential targets	Susceptible to	Ref
Hepatitis A virus	Virus adsorption and penetration into the host cell	*Mentha longifolia* (Lamiaceae)	1
Hepatitis A virus	Virus adsorption and penetration into the host cell	*Ocimum basilicum* (Lamiaceae)	1
Coxsackie B virus	Virus adsorption and penetration into the host cell	*Mentha longifolia* (Lamiaceae)	1
HIV	Protease	*Agastache rugosa* (Lamiaceae)	23
HIV	Protease	*Crataegus pinnatifida* (Rosaceae)	23
HIV	Reverse transcriptase Inhibition in syncytium	*Garcinia speciosa* (Clusiaceae)	23
HIV	Inhibited replication	*Vatica cinerea* (Dipterocarpaceae)	23
HIV	Reverse transcriptase infection/entry, replication	*Scutellaria baicalensis* (Lamiaceae)	23
HIV	Reverse Transcriptase	*Calophyllum lanigerum* (Solanaceae)	23
Influenza virus	Sialidase	*Ginkgo biloba* (Ginkgoaceae)	23
Influenza virus	Sialidase	*Scutellaria baicalensis* (Lamiaceae)	23
Influenza virus	Virus replication	*Uncaria rhynchophylla* (Rubiaceae)	23
Human, Avian, equine strains of influenza A virus	Early stage viral replication	*Geranium sanguineum* (Geraniaceae)	39
Influenza viruses A & B (FluV A/B) (Orthomyxoviridae)	Hemagglutinin, Neuraminidase	*Echinaceae* (Asteraceae)	37
Respiratory syncytial virus (Paramyxoviridae)	Membrane components	*Echinaceae* (Asteraceae)	37
Coronaviruses (HcoV, SARS CoV) (Coronaviridae)	Membrane components	*Echinaceae* (Asteraceae)	37
Rhinoviruses, Coxsackieviruses (Picornaviridae)	Capsid proteins, Replication	*Echinaceae* (Asteraceae)	37
Herpes viruses (HSV.1/2) (Herpesviridae)	Membrane components, virus replication	*Echinaceae* (Asteraceae)	37
Various strains of Influenza A & B	Hemagglutinin, Neuraminidase, Viral RNA synthesis and virus adsorption	*Camellia sinensis* (Theaceae)	39
Human and Avian Influenza virus	Early stage virus replication by binding to the virus and preventing entry into the cells	*Cistus incanus* (Ciataceae)	39
Herpes simplex virus	Replication of virus	*Caesalpinia pulcheerima* (Fabaceae)	47
Adenoidal-pharyngeal-conjuctival (APC) virus or adeno virus	Inhibited adenovirus infection and virulent adenain protein	*Camellia sinensis*(Theaceae)	40
Epstein –Barr virus	Inhibited the expression of EBV lytic protein	*Camellia sinensis*(Theaceae)	40
HIV -1	Blocking HIV-1 envelope glycoprotein-mediated membrane fusion	*Camellia sinensis*(Theaceae)	40
Influenza virus	Bound to viral hemagglutinin	*Camellia sinensis* (Theaceae)	40

Table 7: Solvents used for active components extraction[28]

Water	Ethanol	Methanol	Chloroform	Di-chloro methanol	Ether	Acetone
Anthocyanins	Tannins	Anthocyanins	Terpenoids	Terpenoids	Alkaloids	Flavanols
Starches	Polyphenols	Terpenoids	Flavonoids		Terpenoids	
Tannins	Polyacetylenes	Saponins			Coumarins	
Saponins	Flavanol	Tannins			Fatty acids	
Terpenoids	Terpenoids	Xanthophyllines				
Polypeptides	Sterols	Totarol				
Lectins	Alkaloids	Quassinoids				
	Propolis	Lactones				
		Flavones				
		Phenones				
		Poly-phenols				

Adapted from cowan (1999)

Table 8: Protein responsible for resistance against some antiviral drugs[48]

Antiviral agent	Altered Protein Conferring Resistance
Acyclovir	viral thymidine kinase
	viral DNA polymerase
Penciclovir	viral thymidine kinase
	viral DNA polymerase
Foscarnet	viral DNA polymerase
Vidarabine	viral DNA polymerase
Ganciclovir	viral UL97 phosphotransferase
	viral DNA polymerase
Amantadine	viral M2 protein (ion channel)
Rimantadine	viral M2 protein (ion channel)
Nucleoside RT inhibitors	viral reverse transcriptase
Non-nucleoside RT inhibitors	viral reverse transcriptase
Protease inhibitors	viral protease

Assays for Screening New Drugs

Drug screening is essential for the discovery of antiviral compounds. Diverse *in vitro* antiviral assays exist and most are cell-based including cytopathic effect assay (measurement of plaque reduction) and MTT assay (measurement of cell variability). Other assays, such as ELISA, are also frequently used to detect the presence of adenovirus protein for Cytotoxicity study of the drug. These antiviral assays are not standardized and time-consuming and therefore, other new methods are increasingly used for drug screening[35].

New Methods for Drug Screening

RT-PCR method

More recently real time PCR-based antiviral assay have been used and were shown to be a more rapid and effective drug-screening test. Some caution should be taken since in other assays with RT-PCR, it can be shown that some pathogens have cross-reactions in certain assays. With the use of real time PCR, the antiviral assay becomes rapid, reproducible and could replace classical and more labor-intensive infectivity assays[35].

Biosensor Method using Capacitance Sensor Arrays

The capacitance sensor array could be a new method for antiviral drug screening. This array is used to detect virus entry via receptor-mediated endocytosis, which is also an essential process for therapeutic gene/drug delivery that is targeted to a specific cell type. By screening which compounds act on the virus targeting cell type, new antiviral drugs could be discovered[35].

Computation Method

Bioinformatics and computational methods have been used to discover novel pharmaceuticals. With the bioinformatics tools and software, one can simulate drug-receptor interactions, predict drug bioavailability and bioactivity and illustrate the functional structure of the drug. Computational methods can be applied in antiviral drug screening and recently, p16 (INK4a) peptide mimetics, which inhibit viral cell cycles, have been identified *via* virtual screening[35].

Antiviral Resistance

Development of antiviral resistance is mainly associated with viral fitness and the potency and genetic barrier to resistance of antiviral agents. In general terms, viral fitness is ability of a virus to replicate in a defined environment. Usually wild type virus is "more fit" than mutant virus as far as replication is concerned, but mutant virus have a survival advantage in presence of an antiviral agent. In due course of time, compensatory or secondary mutations rectifies the errors in DNA polymerases of mutant strains and make them capable to replicate at near wild type levels and thus causes development of antiviral resistance[46]. Potency of a drug is defined by time taken by drug to suppress the viral replication. More rapidly a drug suppress the replication, lower the risk of developing antiviral resistance. Drug with a low potency exerts minimal pressure on antiviral population and thus have a low probability of producing antiviral resistance. Similarly a drug with high potency achieve rapid and complete suppression of virus thus again providing little opportunity for antiviral resistance through mutations. Maximum chances for selection of drug resistant virus are against an antiviral agent with modest potency as it incompletely suppresses viral replication. At last, genetic barrier is generally refers to the requirement of number of mutations in order to replicate efficiently in presence of an antiviral agent[46]. The antiviral agents generally inhibit steps in virus-specific replication. This is usually accomplished by the targeting of viral enzymes, thus interfering with viral nucleic acid synthesis. In general, mutations within the viral genome account for the acquisition of antiviral resistance. Single non-lethal nucleotide mutations often result in critical amino acid substitutions in a viral protein[42]. A summarization of various altered proteins responsible for conferring viral resistance is shown in Table 8. Presence of an antiviral agent creates a selection pressure and mutations confer a replication advantage to certain virus which ultimately becomes a predominant virus species[46]. Alternatively, spontaneous mutations may arise during drug exposure. The biological consequences of such viral mutations can include alterations in viral pathogenicity, transmissibility and genetic stability[42]. Within the past decade therapeutic options for viral infections have improved significantly, however, the emergence of resistant viruses is also complicating the scenario. The further disposal of resistant strains is one reason for therapeutic failure[42].

CONCLUSION

In conclusion, there is a much need for the development of novel anti-viral agents. A number of epidemiological and animal model studies have been investigated for cellular and sub-cellular targets of these antivirals and promising results have been observed. Still a lot of work has to be done to further investigation in to its actual potential for human use. This review has revealed a rich source of medicinal and potential targets of many plants extracts. In addition to lacking the adverse side effects of pharmaceutical drugs, advanced herbal formulas tend to be inherently safer, more effective, and less expensive than their synthetic counterparts. In the present scenario, a number of synthetic antiviral drugs are available which proves to be effective against viruses but in a specific manner. Then again, the problem of anti-viral resistance makes most of the antiviral drugs ineffective. Therefore, there is an urgent need for the development of new formulations having effective antiviral properties. Knowledge based on traditional system of medicines can be utilised in development of various herbal formulations from different medicinal plants. The field of herbal medicines holds immense possibilities for research and development and various countries around the world are now relying on their research and development programs for formulation of effective drugs against various viral diseases based on the knowledge of traditional systems on medicines including Ayurveda.

REFERENCES

1. Al-Ali KH and El-Badry AA. Anti-viral activity of two Labiatae plants Naana Hassoi, Habak and Basil Rahan, of Al Madiah Almunawarah. Journal of Medicine and Biomedical Sciences 2010; 1-7.
2. World Health Statistics. World Health Organization; 2012.
3. Simoni IC, Manha APS, Sciessere L, Hoe VMH, Takinami VH and Fernandes MJB. Evaluation of antiviral activity of Brazilian Cerrado plants against animal animal viruses. Virus Review and Research 2007; 12: 1-17.
4. Gupta YK, Briyal S and Gulati A. Therapeutic Potential of Herbal Drugs in Cerebral Ischemia. Indian Journal of Physiology and Pharmacology 2010; 54(2): 99-122. PMid:21090528
5. Uprety Y, Asselin H, Dhakal A and Julien N. Traditional use of medicinal plants in the boreal forest of Canada: review and perspectives. Journal of Ethnobiology and Ethnomedicine 2012; 8: 7. http://dx .doi.org/10.1186/1746-4269-8-7PMid:22289509 PMCid:3316145

6. Kumar BNS, Swamy BNV, Swamy A and Murali A. A review of natural diuretics. Research Journal of Pharmaceutical, Biological and Chemical Sciences 2010; 1(4): 615-634.
7. Faral-Tello P, Mirazo S, Dutra C, Perez A, Geis-Asteggiante L, Frabasile S, Koncke E, Davyt D, Cavallaro L, Heinzen H and Arbiza J. Cytotoxic, virucidal and antiviral activity of South American Plant and Algae extracts. The Scientific World Journal 2012; 174837: 1-5. http://dx.doi.org/10.1100/2012/174837PMid:22619617 PMCid:3349323
8. Rathore B, Mahdi AA, Paul BN, Saxena PN and Das SK. Indian Herbal Medicines: Possible Potent Therapeutic Agents for Rheumatoid Arthritis. Journal of Clinical Biochemistry and Nutrition 2007; 41: 12-17.http://dx.doi.org/10.3164/jcbn.2007002PMid:18392103 PMCid:2274991
9. Hudson JB. The use of herbal extract in use control of influenza. Journal of Medicinal Plants Research 2009; 3(13): 1189-1195.
10. Ayoka AO, Akomolafe RO, Akinsomisoye OS and Ukponmwan OE. Medicinal and economical value of Spondias mombin. African Journal of Biomedical Research 2008; 11: 129-136.
11. Abonyi DO, Adikwu MU, Esimone CO and Ibezim EC. Plants as source of antiviral agents. African Journal of Biotechnology 2009; 8(17): 3989-3994.
12. Edziri H, Mastouri M, Mahjoub MA, Ammar S, Mighri Z, Gutmann L and Aouni M. Antiviral activity of leaves extracts of *Marrubium alysson* L. Journal of Medicinal Plants Research 2011; 5(3): 360-363.
13. Balasubramanian G, Sarathi M, Kumar SR, Hameed ASS. Screening the antiviral activity of Indian medicinal plants against white spot syndrome virus in shrimp. Aquaculture 2007; 263: 15-19. http://dx.doi.org/10.1016/j.aquaculture.2006.09.037
14. Merina N, Chandra KJ and Jibon K. Medicinal plants with potential anticancer activities: A Review. International Research Journal of Pharmacy 2012; 3(6): 26-30.
15. Borokini TI and Omotayo FO. Photochemical and ethnobotanical study of some selected medicinal plants from Nigeria. Journal of Medicinal Plants Research 2012; 6(7): 1106-1118.
16. Perera C and Efferth T. Antiviral medicinal herbs and phytochemicals. Journal of Pharmacogonosy 2012; 3(1): 45-48.
17. Clercq Erik DE. Molecular Targets for Antiviral Agents. Journal of Pharmacology and Experimental Therapeutics 2001; 297(1): 1-10.
18. Fernandes MJB, Barros AV, Melo MS and Simoni IC. Screening of Brazilian plants for antiviral activity against animal herpesviruses. Journal of Medicinal Plants Research 2012; 6(12): 2261-2265.
19. Microbiologybytes.com; homepage on internet. Virology: Antivirals: Antiviral Drugs, Available from: http://www.microbiologybytes.com/virology/Antivirals.html. Updated 2009; 08.
20. Boriskin YS, Leneva IA, Pécheur EI and Polyak SJ. Arbidol: A Broad Spectrum Antiviral Compound that Blocks Viral Fusion. Current Medicinal Chemistry 2008; 15(5): 1-9.
21. Sumithira P, Mangala SD, Sophie AM and Latha CP. Antiviral and antioxidant activities of two medicinal plants. International Journal of Current Science 2012; 256-261.
22. Patwardhan B and Gautan M. Botanical immunodrugs: scope and opportunities. Drug Discovery Today 2005; 10: 495-502. http://dx.doi.org/10.1016/S1359-6446(04)03357-4
23. Kitazato K, Wang Y and Kobayashi N. Viral infectious disease and natural products with antiviral activity. Drug Discovery and Therapeutics 2007; 1(1): 14-22.
24. Vijayan P, Raghu C, Ashok G, Dhanaraj SA and Suresh B. Antiviral activity of medicinal plants of Nilgiris. Indian Journal of Medical Research 2004; 120: 24-29. PMid:15299228
25. Prakash P and Gupta N. Therapeutic uses of *Ocimum sanctum* Linn (Tulsi) with a note on Eugenol and its pharmacological actions: A Short Review. Indian Journal of Physiology and Pharmacology 2005; 49(2): 125-131. PMid:16170979
26. Okwu DE and Uchenna NF. Exotic multifaceted medicinal plants of drugs and pharmaceutical industries. African Journal of Biotechnology 2009; 8(25): 7271-7282.
27. Zheng J, He J, Ji B, Li Y and Zhang X. Antihyperglycemic activity of *Prunella vulgaris* L. in streptozotocin-induced diabetic mice. Asia Pacific Journal of Clinical Nutrition 2007; 16(1): 427-431. PMid:17392144
28. Cowan Murphy Marjorie. Plant products as antimicrobial agents. Clinical microbiology reviews 1999; 564-582. PMid:10515903 PMCid:88925
29. Krysko DV, Vanden Berghe T, Parthoens E, Vandenabeele P. Methods for distinguishing apoptotic from necrotic cells and measuring their clearance. Methods Enzymology 2008; 442: 307-41. http://dx.doi.org/10.1016/S0076-6879(08)01416-X
30. Stoddart MJ. Mammalian Cell Viability: Methods and Protocols Vol: 740.
31. Riss TL and Moravec RA. Use of multiple assay endpoints to investigate the effects of incubation time, dose of toxin, and plating density in cell-based cytotoxicity assays. Assay Drug Dev Technol 2004; 2(1): 51–62. http://dx.doi.org/10.1089/154065804322966315 PMid:15090210
32. Weyermann J, Lochmann D and Zimmer A. A practical note on the use of cytotoxicity assays. International Journal of Pharmaceutics 2005; 288: 369-376.http://dx.doi.org/10.1016/j.ijpharm.2004.09.018 PMid:15620877
33. Decker T and Lohmann-Matthes ML. A quick and simple method for the quantitation of lactate dehydrogenase release in measurements of cellular cytotoxicity and tumor necrosis factor (TNF) activity. The Journal of Immunology. Methods 1988; 115(1): 61–9. http://dx.doi.org/10.1016/0022-1759(88)90310-9
34. Niles AL, Moravec RA, Eric Hesselberth P, Scurria MA, Daily WJ and Riss TL. A homogeneous assay to measure live and dead cells in the same sample by detecting different protease markers. Analytical Biochemistry 2007; 366(2): 197–206. http://dx.doi.org/10.1016/j.ab.2007.04.007 PMid:17512890
35. Waye MMY and Sing CW. Anti-viral Drugs for Human Adenoviruses. Pharmaceuticals 2010; 3: 3343-3354. http://dx.doi.org/10.3390/ph3103343
36. Mukhtar M, Arshad M, Ahmad M, Pomerantz RJ, Wigdahl B and Parveen Z. Antiviral Potential of medicinal plants. Virus Reseacrch 2008; 131: 111-120. http://dx.doi.org/10.1016/j.virusres.2007.09.008 PMid:17981353
37. Hudson J and Vimalanathan S. Echinacea – A source of potent antivirals for respiratory virus infection. Pharmaceuticals 2011; 4: 1019-1031. http://dx.doi.org/10.3390/ph4071019
38. Tang Leon IC and Ling Anna PK. Screening of anti dengue activity in methanolic extracts of medicinal plants. BMC complementary and alternative medicine 2012; 12: 3. http://dx.doi.org/10.1186/1472-6882-12-3 PMid:22244370 PMCid:3269354
39. Hudson JB. The use of herbal extract in use control of influenza. Journal of Medicinal Plants Research 2009; 3(13): 1189-1195.
40. Friedman M. Overview of antibacterial, antitoxin, antiviral and antifungal activities of tea flavonoids and teas. Molecular Nutrition and food Research 2007; 51: 116-134. http://dx.doi.org/10.1002/mnfr.200600173 PMid:17195249
41. Duman R. Antiherpetic activity of some endemic Hypericum species in Turkey. African Journal of Biotechnology 2012; 11(5): 1240-1244.
42. Balasubramanian P, Jayalakshmi K, Vidhya N, Prasad R, Sheriff A Khaleefathullah, Kathiravan G, Rajagopal K and Sureban Sripathi M. Antiviral activity of ancient system of aurvedic medicinal plant *Cissus quadrangularis* L.(Vitaceae). Journal of basic and clinical pharmacy 2010; 1(1): 37-40.
43. Hafidh RR, Abdulamir AS, Jahanshiri F, Abas F, Bakar F Abu and Sekawi Z. Asia is the Mine of Natural Antiviral Products for Public Health. The Open Complementary Medicine Journal 2009; 1: 58-68.
44. Locher CP, Witvrouw M, Béthune MPD, Burch MT, Mower HF, Davis H, Lasure A, Pauwels R, Clercq EDE and Vlietinck AJ. Antiviral activity of Hawaiian medicinal plants against human immunodeficiency virus type-1. Phytomedicine 1996; 2(3): 259-264. http://dx.doi.org/10.1016/S0944-7113(96)80052-3
45. Devi B Parimala and Manoharan K. Anti Viral Medicinal Plants – An Ethnobotanical Approach. Journal of Phytology 2009; 1(6): 417-421.
46. Ghany MG and Doo EC. Antiviral resistance and Hepatitis B therapy. Hepatology 2009; 49(5): S174-S184. http://dx.doi.org/10.1002/hep.22900 PMid:19399794 PMCid:2707848
47. Chiang LC, Chiang W, Liu MC and Lin CC. *In vitro* antiviral activities of *Caesalpinia pulcherrima* and its related flavonoids. Journal of Antimicrobial Chemotherapy 2003; 52: 194-198. http://dx.doi.org/10.1093/jac/dkg291 PMid:12837746
48. Kimberlin DW and Whitley RJ. Antiviral resistance: mechanisms, clinical significance, and future implications. Journal of Antimicrobial Chemotherapy1996;37: 403-421. http://dx.doi.org/ 10.1093/jac/37.3.403 PMid:9182098

Cite this article as:
Ruwali Pushpa, Rai Nishant, Kumar Navin, Gautam Pankaj. Antiviral potential of medicinal plants: An overview. Int. Res. J. Pharm. 2013; 4(6):8-16

Source of support: Nil, Conflict of interest: None Declared