



## A review on-recent approach in antiviral drugs

D Umamaheswari\*, S Dhivagar, G Karthick, S Navaz Aarif Khaan, B S Venkatswaralu

Department of Pharmaceutical Chemistry, Vinayaka Missions College of Pharmacy, Salem, Tamil Nadu, India

### Abstract

In the last twenty years there has been a growing understanding of viral multiplication, which has allowed us to develop new drugs within the battle against viral infections. The aim of this review is to seem at the available antiviral drugs, their use and drawbacks and to debate the therapy of common viral diseases and therefore the possibilities for the near future. A first contamination frequently occurs without serious symptoms or even unrecognized, where after the virus can be latent for many years before expressing itself. Moreover, virus identification is difficult and time-consuming, where quick therapeutic intervention is required to avoid spread of the virus. Nevertheless, we are ready to treat viral infections to a particular extent and a few new developments are promising.

**Keywords:** anti-viral drug, infections, anti-viral approaches

### Introduction

Viruses have too simple a structure to increase themselves. For multiplication, an epidemic invades a cell, using the biochemical mechanisms of this cell to form new viral proteins and genetic material. So, virus and host cell are closely connected and an efficient antiviral must be able to distinguish the virus from the host cell. In the last twenty years there has been a growing understanding of viral multiplication, which has allowed us to develop new drugs within the battle against viral infections<sup>(1)</sup>.

The development and marketing of acyclovir in 1981, was a Threaten in antiviral therapy. Acyclovir is effective in a number of viral herpes diseases with only narrow adverse effects. Mortality and morbidity of herpes Infections have decreased dramatically.

Together the increasing uses of immunosuppressive drugs, bacterial and viral infections have become a more pronounced problem and require the development of new drugs.

This process was accelerated by the human immune deficiency virus (HIV) outbreak, which required anti-HIV drugs and antiviral drugs for viral infections secondary to AIDS. At this moment enormous amounts of cash and time are spent within the research for brand spanking new antiviral drugs.

The aim of this review is to seem at the available antiviral drugs, their use and drawbacks and to debate the therapy of common viral diseases and therefore the possibilities for the near future<sup>(2)</sup>.

### Mosquito Transmission Cycle

- Uninfected mosquito. A mosquito becomes infected by feeding on a person who has malaria.
- Transmission of parasite. If this mosquito bites you within the longer term, it can transmit malaria parasites to you.
- In the liver. Once the parasites enter your body, they visit your liver where some types can lie dormant for as long as a year.

- Into the bloodstream. When the parasites mature, they leave the liver and infect your red blood cells. This is when people typically establish malaria symptoms.
- On to the next person. If an uninfected mosquito bite you at this point in the cycle, it will become infected with your malaria parasites and can spread them to the other people it bites.
- Malaria may be a disease caused by a parasite. The parasite is circulate to humans through the bites of infected mosquitoes. People who have malaria usually feel very sick with a high fever and shaking chills.
- While the disease is rare in temperate climates, malaria remains common in tropical and subtropical countries. Each year nearly 290 million people are infected with malaria, and quite 400,000 people die of the disease.

To reduce malaria infections, world health programs distribute preventive drugs and insecticide-treated bed nets to guard people from mosquito<sup>(3)</sup>.

### Antiviral drug Classification

- DNA polymerase inhibitors — Purine Nucleoside Analogues: Acyclovir, Ganciclovir, Famiciclovir, Valacyclovir, Penciclovir,
- Cidofovir – Pyrimidine
- Nucleoside Analogues: Idoxuridine – Non nucleoside Foscarnet
- Inhibitors of viral penetration Amantadine, Rimantadine.
- m-RNA Synthesis inhibitors Ribvirin, formivirsen.
- Neuraminidase Inhibitors Zanamivir, Oseltamivir.
- Immunomodulators Immunoglobulins, Interferons, Palivizumab, Imiquimod<sup>(4)</sup>.

### Literature Review

Tatyana A Shamliyan *et al.* Developed the Systematic review of the literature on comparative effectiveness of antiviral treatments for chronic hepatitis B infections. Individual clinical decisions should rely on comparative effectiveness and absolute rates of intermediate outcomes and adverse

events. Future research should clarify the relationship of intermediate and clinical outcomes and cost-effectiveness of drugs for evidence-based policy and clinical decisions<sup>[5]</sup>.

*E.H.H. Wiltin et al.* method for Viruses has too simple a structure to multiply them. For multiplication, a virus invades a cell, using the biochemical mechanisms of this cell to make new viral proteins and genetic material. So, virus and host cell are intimately connected and an effective antiviral drug must be able to distinguish the virus from the host cell. In the last twenty years there has been a growing understanding of viral multiplication, which has allowed us to develop new drugs in the battle against viral infections<sup>[6]</sup>.

*Shamaila kausar et al.* Developed Tiviral drugs are a class of medicines particularly used for the treatment of viral infections. Drugs that combat viral infections are called antiviral drugs. Viruses are among the major pathogenic agents that cause number of serious diseases in humans, animals and plants. Viruses cause many diseases in humans, from self-resolving diseases to acute fatal diseases. Developing strategies for the antiviral drugs are focused on two different approaches: Targeting the viruses themselves or the host cell factors. Antiviral drugs that directly target the viruses include the inhibitors of virus attachment, inhibitors of virus entry, uncoating inhibitors, polymerase inhibitors, protease inhibitors, Inhibitors of nucleoside and nucleotide reverse transcriptase and the inhibitors of integrase. The inhibitors of protease (ritonavir, atazanavir and darunavir), viral DNA polymerase (acyclovir, tenofovir, valganciclovir and valacyclovir) and of integrase (raltegravir) are listed among the Top 200 Drugs by sales during 2010s. Still no effective antiviral drugs are available for many viral infections. Though, there are a couple of drugs for herpesviruses, many for influenza and some new antiviral drugs for treating hepatitis C infection and HIV. Action mechanism of antiviral drugs consists of its transformation to triphosphate following the viral DNA synthesis inhibition. An analysis of the action mechanism of known antiviral drugs concluded that they can increase the cell's resistance to a virus (interferons), suppress the virus adsorption in the cell or its diffusion into the cell and its deproteinisation process in the cell (amantadine) along with antimetabolites that causes the inhibition of nucleic acids synthesis. This review will address currently used antiviral drugs, mechanism of action and antiviral agents reported against COVID-19<sup>[7]</sup>.

*O.L. Bryan-Marrugo et al.* Developed Antiviral therapy is a well-established discipline with a promising future. Based on economic, scientific and medical interest, and a continuous need for new drugs to avoid resistance, it is most likely that the development of antiviral drugs over the next 20 years will be focused on HIV and HCV. Today, well-established diagnostic and study systems are available for HCV and other viruses. New targets against HCV, such as inhibitors for the scavenger receptor type B1 (SR-B1) and CD81, neutralizing antibodies against the viral glycoproteins and the NS5B polymerase, as well as the NS2/3 auto-protease, the NS3 helicase, and non-enzymatic targets such as NS4B and NS5A proteins are in development. Other potential drugs targeting HCV replication include compounds active against the IRES element and antisense inhibition. As mentioned before, virus factors are not the only potential targets for inhibition, but host targets are as well, including microRNAs, cellular receptors, adhesion molecules and cyclophilins. For the near

future, a combination of host and viral inhibitors will provide a variety of drug Regimes appropriate for different patients that could lead to interferon-free therapies that can consistently clear the infection<sup>[8]</sup>.

*Catherine S. Adamson et al.* Method for The one-virus-one-drug approach to antiviral discovery and development has been successful, but only if the viral disease satisfies the medical and economic criteria required to drive the substantial research effort, financial investment and political will, essential for delivering an effective clinically approved antiviral drug. The global campaign to find SARS-CoV-2 antivirals will undoubtedly result in the development innovative approaches to screening, accelerated clinical testing and rapid manufacturing scale-up to bring these compounds to the market as quickly as possible. Are we prepared for the next viral pandemic? The answer is still "no". The catastrophic impact of the SARS-CoV-2 pandemic has the potential to divert attention away from other viruses that cause human disease and have the potential to cause the next pandemic. To mitigate this risk, there needs to be continued surveillance and modelling to support the prediction of which deadly virus will be the next to emerge into the human population. Of critical importance is directing research effort and investment into the development of broadly-acting antivirals that can be mobilised as the first line of defence upon emergence of new viral Pathogens<sup>[9]</sup>.

*Shamaila Kausar et al.* Developed the fight between human and viruses in on and both are rapidly improving the strategies of attacking and defence. In recent years, there has been tremendous progress in understanding the genetic basis and molecular mechanism of diseases. Various new drugs have been formulated and the development of a lot more is in underway. Though, the new infectious diseases caused by viruses such as COVID-19 remain a challenge. Furthermore, the drugs failure in human trials is a general process that requires be working out and addressing<sup>[10]</sup>.

*Sara M Thomasy et al.* Method for Feline herpesvirus type 1 (FHV-1) is a common and important cause of ocular surface disease, dermatitis, respiratory disease, and potentially intraocular disease in cats. Many antiviral drugs developed for the treatment of humans infected with herpesviruses have been used to treat cats infected with FHV-1. Translational use of drugs in this manner ideally requires methodical investigation of their in vitro efficacy against FHV-1 followed by pharmacokinetic and safety trials in normal cats. Subsequently, placebo-controlled efficacy studies in experimentally inoculated animals should be performed followed, finally, by carefully designed and monitored clinical trials in client-owned animals<sup>[11]</sup>.

*R A Perveen et al.* Developed several attempts to find effective antiviral drugs against the COVID-19. Although majority of the COVID-19 patients have mild to moderate clinical events, up to 5-10% may have severe, life threatening events that urgently require effective drugs. Total of five RCTs on 439 patients and seventeen case series involving 1656 patients were found in the specified review period that reported the use of Lopinavir, Ritonavir, Remdesivir, Oseltamivir, Ribavirin in patients with COVID-19; but none of which showed efficacy of antiviral therapy. Such current findings impede researchers from recommending an appropriate and effective antiviral therapy against COVID-19, making it a serious concern for the global community<sup>[12]</sup>.

*Fatemeh Heidary et al.* Method for Ivermectin, owing to its antiviral activity, may play a pivotal role in several essential biological processes; therefore it could serve as a potential candidate in the treatment of different types of viruses including COVID-19. Clinical trials are necessary to appraise the effects of ivermectin on COVID-19 in clinical setting and this warrants additional investigation for probable benefits in humans in the current and future pandemics. Moreover, further trials are needed to confirm the safety and efficacy of ivermectin for human use against COVID-19 to discover preventive or therapeutic window. If safe formulations or analogs can be derived that can be administered to achieve therapeutic concentrations, ivermectin could be useful as a broad-spectrum antiviral agent <sup>[13]</sup>.

*Patrick R Ching et al.* Developed Remdesivir is an antiviral used for the treatment of COVID-19 requiring hospitalisation. Information on its cardiovascular safety profile is scarce. We report the case of a 37-year-old man with COVID-19 who developed bradycardia after receiving remdesivir. We recommend a baseline ECG for all patients prior to receiving remdesivir and continuous cardiac monitoring during treatment, especially among those with underlying cardiovascular disease, elderly and using  $\beta$ -blockers <sup>[14]</sup>.

*Muhammed Abdel-Hamied Abdel-Tawab et al.* Method for Sofosbuvir is a direct-acting antiviral drug that inhibits hepatitis C virus (HCV) NS5B polymerase which in turn reflects on the virus replication inside biological systems. The vital importance of sofosbuvir is not only based on its effect on HCV but also on other lethal viruses such as Zika and SARS-COVID-19. Accordingly, there is a continuous shedding of light on the development and validation of accurate and fast analytical methods for the determination of sofosbuvir in different environments <sup>[15]</sup>.

*Elizabeth Oyinkansola Omotola et al.* Developed Antiretroviral drugs for the treatment of human immunodeficiency virus (HIV) and other viral infections are among the emerging contaminants considered for ecological risk assessment. These compounds have been reported to be widely distributed in water bodies and other aquatic environments, while data concerning the risk they may pose to unintended non-target species in a different ecosystem (environment) is scanty. In South Africa and other developing countries, lamivudine is one of the common antiretrovirals applied. At lower concentrations of 10  $\mu\text{g/L}$  lamivudine, 90% and 55% survival rates were observed at 24 h and 48 h, respectively. No potential mutagenic effects were observed from the Ames test at both concentrations of lamivudine. This impact was further investigated through microscopic examination, revealing some chromosomal aberration in the exposed *Allium cepa* root tips. The *Lactuca sativa* bioassay showed a slight adverse impact on both the germination rate of the seeds and their respective hypocotyl lengths compared to the control. Overall, this indicates that lamivudine poses an ecological health risk at different trophic levels, to both flora and fauna, at concentrations previously found in the environment <sup>[16]</sup>.

*Cassandra Pardini et al.* suggest that Antiviral agents used to treat seasonal influenza shorten the time to alleviation of influenza symptoms (TTAS), according to the findings of a systematic review and network meta-analysis recently published in JAMA Network Open.

The 4 antiviral agents approved by the Food and Drug Administration for the treatment of seasonal influenza include the neuraminidase inhibitors oseltamivir, zanamivir, and peramivir, and the polymerase acidic endonuclease inhibitor, baloxavir marboxil. To evaluate the safety and efficacy in treating seasonal influenza in healthy adults and children, the authors analyzed randomized clinical trials evaluating these agents compared with other active agents or placebo. The main outcomes of the study included TTAS, influenza complications, and adverse events <sup>[17]</sup>.

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*Kaasam et al.* estimated Hepatitis C virus (HCV) infection is known to be one of the leading causes of hepatocellular carcinoma (HCC) all over the world. Previously, multiple studies have confirmed a decreased rate of HCC occurrence or recurrence in the cases of hepatitis C associated cirrhosis after treatment with interferon, in comparison to the untreated cases, even in the absence of clearance of HCV. Treatment programs with direct-acting antivirals (DAAs) as a new method for HCV treatment and cure in 2014, with higher safety and efficacy, were considered as an important step in the treatment of patients with history of HCC, improving their overall prognosis. Recently, reports coming from various European centers claimed that the risk of HCC increased following DAAs therapy, especially in cases with previous HCC. Moreover, other studies revealed that the recurrence of HCC after DAAs treatment was more aggressive <sup>[19]</sup>.

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