

# Mechanism of Action of Acyclovir with its Different dosage form: A Review

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**Abstract :** Antiviral drugs are a class of medicines particularly used for the treatment of viral infections. Drugs that combat viral infections are called antiviral drugs. Acyclovir (ACV) has a novel, highly selective biological activity which results in the inhibition of herpes virus replication at concentrations 300–3000-fold lower than those that will inhibit mammalian cellular functions. Viruses are among the major pathogenic agents that cause number of serious diseases in humans, animals and plants. 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. Acyclovir is available in different dosage forms in the market such in the form of tablets , capsules, syrups, creams etc.

**Keywords:** Acyclovir, antiviral drug, mechanism of action, viruses.

## INTRODUCTION

Infectious diseases are well known since ancient time to human civilisation. Infectious disease are caused due to different microorganisms such as bacteria, viruses and fungi<sup>1</sup>. Viral structure is simple and consists of a protein coat, nucleic acid, viral enzymes and, sometimes, a lipid envelope, unlike the complex structure of fungi, helminths and protozoa. Additionally, viruses use the host's cellular machinery for replication, hence are obligate intracellular pathogens. Such characteristics create the difficulties in developing drugs with selective toxicity against viruses.<sup>2</sup> Viruses are ultra microscopic agents having either DNA or RNA as the genetic material and are known to cause variety of diseases in humans, animals and plants. The fight between humans and viruses is continuous process, as both will adopt different strategies to fight against each other. Antiviral drugs development is a tedious process involving many stages such as target identification and screening, lead generation and optimisation, clinical studies and the drug registration, etc.<sup>3</sup>

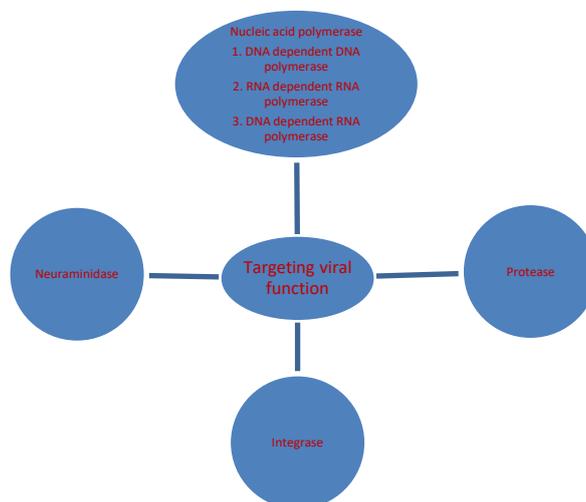
Antiviral drugs are a class of medicines particularly used for the treatment of viral infections. Specific antiviral drugs are used for treating specific viruses just like the antibiotics for bacteria. Antiviral drugs, unlike the most antibiotics, do not destroy their target pathogens; rather inhibit their development. As the viruses use the host's cells to replicate, hence makes it difficult to design a safe and effective antiviral drug. Therefore, it is difficult to find the drug targets that would interfere with the virus without damaging the host's cells. Furthermore, the major complications in developing anti-viral drugs and vaccines are because of viral variation<sup>4-5</sup>. With increase in the awareness about the viruses, their mechanism of infection and the rapid evolvement of novel strategies and techniques for antiviral will speed up the novel antiviral drugs development.<sup>6-7</sup>

### Steps of viral infections:

The virus attaches to a host cell injecting its genetic material into the host cell during attachment and penetration stage.

- In the next step, the viral DNA or RNA is itself incorporated into the genetic material of the host cell inducing it to replicate the viral genome. This step involves the uncoating, replication and assembly during the virus life cycle.
- During release, the host cell releases the newly created viruses, either through the breakage of the cell, waiting cell death or by budding off through the cell membrane.<sup>8-9</sup>

Figure No:1 Common inhibitory action of antiviral drugs.



### Antiviral medication and its mechanism of action Acyclovir 9-15

The hidden development of this methodology, an increase in acyclovir monophosphate, is catalysed by thymidine kinase caused by cells contaminated by herpes simplex infection or varicella zoster infection or phosphotransferase made by cytomegalovirus. Cellular protein then adds phosphate to produce acyclovir diphosphate and acyclovir triphosphate. Acyclovir triphosphate slows the mixing of viral DNA by countering 2'-deoxy guanosin triphosphate as a substrate for viral DNA polymerase. After acyclovir (not 2'-deoxiguanosin) was implanted in a duplicate of viral DNA, fusion stopped. The acyclovir monophosphate circuit into viral DNA is irreversible, given the way exonuclease bound to polymerases 3', 5' cannot separate them. In this technique, viral DNA polymerase is inactivated in the same way. Acyclovir triphosphate is 30 times greater than herpes simplex type 1 DNA polymerase inhibitors than human alpha-DNA polymerase cells. The small formation of acyclovir triphosphate in uninfected cells and its expression for DNA viral load results in harmless cellular toxic effects. In addition, more than 80% of acyclovir that appears during diffusion is unaffected in the urine. The 50% central acyclovir inhibitory group in contradiction of herpes simplex disease type 1 is 0.1µM, and 0.4µM against herpes simplex disease type 216 and 47.1µM against cytomegalovirus.<sup>15</sup> Even with reduced oral bioavailability, obsession with plasma acyclovir exceeds 50% inhibitory concentration for type 1 and 2 herpes simplex contamination that grows in adults after a combination of 200mg d 'Acyclovir, on the other hand, 800mg is very important to provide plasma obsession over the centre 50% inhibitory concentration for varicella zoster virus. Acyclovir with a fairly short half-life of plasma, 7.7mg should be given every 4–6h for patients damaged by varicella-zoster infection. Acyclovir has been shown to be suitable for the treatment of pollution resulting from contamination with herpes simplex types 1 and 218 and varicella-zoster virus and to disguise specific types of cytomegalovirus.

### MECHANISM OF ACTION OF DRUG: 16

Acyclovir is converted to its triphosphate form, acyclovir triphosphate (ACV-TP), which competitively inhibits viral DNA polymerase, incorporates into and terminates the growing viral DNA chain, and inactivates the viral DNA polymerase.

**Pharmacodynamics:** No relationship has been established between the effective in vitro and in vivo concentrations of acyclovir, although there is a significant correlation between the LD50 of acyclovir for the virus and the clinical response.

**Pharmacokinetics:** Acyclovir is slowly and poorly absorbed from the gastrointestinal tract and bioavailability decreases with increasing dose. Acyclovir is widely distributed into tissues and body fluids. Plasma protein binding is relatively low at 9 to 24%. Renal excretion is the major route of elimination of acyclovir.

**Adverse Effects:** Most common with oral acyclovir are headache, diarrhea, nausea, vomiting and abdominal pain. The most common effects associated with parenteral acyclovir are lightheadedness and anorexia. The most common adverse effects associated with topical acyclovir are mild pain, burning and stinging.

**Dosage:** Capsule 200mg, Cream 5%, Ointment 5%, Oral Suspension 25mg/ml, 50mg/ml, 200mg/5ml Powder for Injection 500mg, Tablet 400mg, 800mg

### Formulation method of tablets by Direct compression method 17-20

All the ingredients (Microcrystalline cellulose, Magnesium Stearate, Sodium Starch Glycolate) were first passed through sieve no 60 and dried for one hour at 60°C and weighed accurately. Drug was mixed with microcrystalline cellulose (MCC) Magnesium Stearate, Sodium Starch Glycolate, and mixing was done for 15 minutes to ensure uniform distribution. All other ingredients were added, tablet weight and hardness was adjusted to 400mg and 5-7 kg/cm<sup>2</sup>, respectively and tablets were punched using single punch machine in a room where humidity was controlled with the help of dehumidifier which was kept on 45 min prior to punching of tablets.

### Evaluation parameters:

1. Appearance : such as tablet size, shape, colour, presence or absence of odour, taste, surface texture and physical flows
2. Hardness: i.e. Hardness or tablet crushing strength was measured using Monsanto tablet hardness tester. The hardness was measured in terms of kg/cm<sup>2</sup>.
3. Thickness : measured by using vernier calipers.
4. Weight variation
5. Friability

### CONCLUSION

In the present study two techniques direct compression and wet granulation were evaluated for their potential for the development of tablets, it can be concluded that the direct compression serves to be a better method for this purpose. Acyclovir is being shown to be effective against certain herpes virus infections especially herpes simplex. Opportunities to treat viral diseases with relatively non-toxic agents are so far rare and experience on the best way to do so, limited. Better results can be expected for certain infections when inclusion criteria are more clearly defined.

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