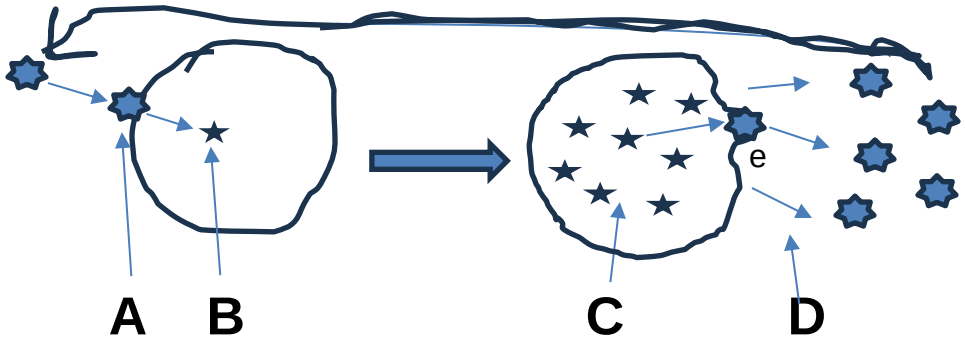
UNDERSTANDING THE HERPESVIRUS

Stages of Viral Infection



A- Viral Fusion to cell membrane
B- Viral Entry into cell (sheds envelope and becomes nucleocapsid (★)
C- Viral Replication (intracellular – in the nucleus)
D- Viral Exit from cell (exocytosis = e) newly formed virions are now able to infect more cells → repeat steps A, B, C & D → exponential replication

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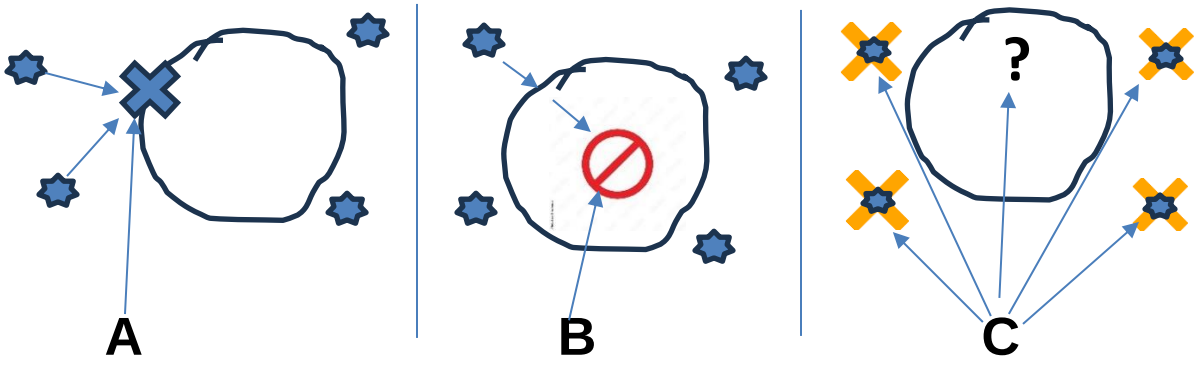
Therapeutic Viral Targeting



A- Docosanol – Extracellular effect - blocks viral fusion with cell membrane
Viral particles (virions) are not killed → potential to spread
B- Antiviral Medications (e.g., nucleoside analogues) - Intracellular effects

Block viral DNA replication ➡ block viral replication
Any remaining extracellular virions are not killed → potential to spread
C- Zap-H™ - Extracellular ((possible intracellular)- disrupts viral membrane
Together with immune system → virions are eradicated / killed

- **NO Viral Fusion**
- **NO Viral Entry or Replication**
- **NO progression to other cells**

BACKGROUND ON THE HERPESVIRUS

HerpesVirus Structure and Relation to Replication

The structure of the herpesvirus comprises an inner core of DNA, surrounded by an outer envelope (also called the viral membrane), which makes up the viral particle, also called a virion. In this way, it is classified as both a DNA virus and an enveloped virus. Viral DNA is stabilized by a shell of proteins called the capsid. Together, the DNA and capsid are referred to as the nucleocapsid. The nucleocapsid is surrounded by the outer envelope, which is formed from the host cell membrane.

The virus is always surrounded by this envelope except after it enters a cell. Upon fusion with the host cell membrane and subsequent cell entry the nuclear material, nucleocapsid, is released. The released nucleocapsid enters the host nucleus, which contains the host DNA. Viral DNA replicates in the nucleus, while simultaneously facilitating the manufacture of its proteins, i.e., the capsid, by manipulating host cell processes and utilizing intracellular organelles. After subsequent release from the nucleus, the newly formed nucleocapsid particles fuse with, and acquire a part of, the host cell outer membrane. In this way, a part of the host cell membrane becomes the viral envelope for all the newly formed viral particles. The enveloped viral particles are then released by a budding mechanism called exocytosis. The greatly expanded number of viral particles that are released from the cell can now spread to other cells, repeating the replication process, expanding exponentially at a rapid pace.

The herpesvirus particles have a predilection for neurons near the base of the brain, in an area called the trigeminal ganglion. The virus lies dormant within these nerve cells and can do so for months to many years, even 30 or more. It can be activated by numerous factors, which can vary between each individual. Triggering factors include stress, lack of sleep, exposure to sun, cold wind, a cold, flu or other illness, a weak immune system, and changing hormone levels.

Why are herpesvirus cold sores/ fever blisters are difficult to treat

The herpesvirus HSV-1 is the main cause of cold sores/fever blisters on lips. A similar herpesvirus, HSV2, is the main cause of genital herpes, but either one of these 2 versions can cause oral cold sores. Herpesvirus owes its successful spread to its complexity, which has enabled it to effectively slow down the human immune system in several different ways. Glycoproteins of the herpesvirus envelope play a significant role in the early interactions, attachment, and entry of viral particles into the host cell. They modulate the immune system to maintain a presence in the infected host. They maintain a balance between preventing being killed by the immune system and preventing host cell death, as their survival depends on host cell survival. Herpesviruses have evolved a mechanism to remain dormant in the body for long periods of time, wherein they linger in a hibernation state known as viral latency.

Why cold sore treatments have limited effectiveness.

In addition to having developed methods by which to hide itself from the immune system, HSV1 infection therapies have had limited success for one particular reason - current treatment methods do not target the virus directly. For example, many cold sore treatments focus on relieving the symptoms, namely itch, tingling and pain, where the effects are typically of temporary nature. Second, treatments are available that block viral entry into host cells, however there is no direct effect on HSV1, and the virions can survive. Third, treatments are available that prevent viral replication, but again the virions can survive. A common denominator for all these treatment methods is that they do not eradicate, disrupt or kill the viral particles themselves.

The immune system is left to deal with the virus on its own, where the lesions and subsequent scab typically last anywhere from 7-14 days, and up to 3-4 weeks in some cases, especially in an individual with a compromised immune system. Whereas treatments that focus on relieving symptoms have no effect on cold sore duration, treatments that block viral entry and those that prevent replication can reduce the duration of a cold sore lesion.

There are limitations for viral entry blocking agents and antiviral medications. For example, a viral entry blocking agent reduces the duration of a cold sore an average of 18 hours (*). A 3/4 of a day reduction in duration is a relatively minor improvement for a lesion that lasts 7-14 days, and longer in immune compromised individuals. Second, an antiviral medication (e.g., nucleoside analogue), "….only reduces the healing process in little more than 2 days (time to loss of scab), from 7.9 days (placebo) to 5.8 days,…**).

* Sacks, SL. et al; Clinical efficacy of topical docosanol 10% cream for herpes simplex labialis: A multicenter, randomized, placebo-controlled trial. J Amer Acad Dermatol. 2001 Aug; 45(2): 222 - 230

** Álvarez DM, Castillo E, et al; Current Antivirals and Novel Botanical Molecules Interfering With Herpes Simplex Virus Infection. Front Microbiol. 2020 Feb 11;11:139. doi: 10.3389/fmicb.2020.00139. PMID: 32117158; PMCID: PMC7026011.

Another issue pertaining to both viral entry blocking agents and antiviral medications is that they need to be started within 24-48 hours of the onset of symptoms, i.e., the sensation of tingling or a small red discoloration along the lip line. After 2 days of symptoms, the viral particles have proliferated to the extent that further treatment with these becomes futile.

Antiviral medications are slightly more effective in reducing duration of symptoms than viral entry blocking agents. However, a further potential problem with antiviral medications is that repetitive use can lead to viral resistance to these medications, making them less effective, or even ineffective. The development of resistance is most common in immune compromised individuals who have a more difficult time eradiating cold sores, and thus they require more frequent use of antiviral medications, leading to resistance.

The Zap-H™ Benefit

Zap-H™ consists of ingredients that together generate synergistic viral envelope disruption resulting in viral killing that is not possible with any single compound acting alone. Fatty acids/oils have long been known to have antiviral properties but are not nearly as effective as the proprietary combination of ingredients in Zap-H™, which generate synergistic improvement over ingredients present in mother's milk and/or plant oils alone. Viral envelope disruption is also theorized to expose hidden virus markers, that can subsequently be targeted by the immune system. Furthermore, fatty acids/ oils have antimicrobial effects against pathogenic bacteria, such as Staphylococcus aureus, but they do not kill beneficial bacteria, such as Bifidobacteria and Lactobacilli. Fatty acids also have biofilm disrupting effects (see below) against numerous bacterial biofilms. Just as for viruses, such biofilm disrupting effects are enhanced with the Zap-H™ formulation. Fatty acids can also reduce inflammation, which can contribute to pathogenic microbial growth. In addition, the anti-inflammatory features can reduce symptoms and and help to reduce the healing time of the scab, which is a form of a wound. Finally, Zap-H™ is formulated for rapid skin absorption, as clinical effectiveness is dependent on the ability of active ingredients to penetrate through the skin, where the viral particles are located.

Mechanism of action and what it means

Combining the information from our lab studies and existing publications, it is thought that a key mechanism of action for Zap-H™ is the ability of its ingredients to disrupt the protective viral envelope. Once the viral envelope is disrupted, it exposes the herpesvirus internal components, which can then be targeted by the body's immune system. This gives the immune system the opportunity to eradicate the virus more effectively. Furthermore, because the immune system can now identify viral molecular targets that have been exposed, it allows the immune system to learn how to build protective measures against the virus. These learned protective measures help the body to prevent the frequency and severity of any potential future outbreaks.

What's a viral envelope and why do I care?

The viral envelope (also called viral membrane) protects the HSV DNA, and its ability to exist and replicate. Disrupting the viral envelope can lead to either direct killing of the virus by Zap-H™ or it can enhance the immune system's ability to target and kill the HSV particles. It is well established that different fatty acids can kill numerous viruses, and this is accomplished by disrupting their viral envelopes, or membranes *.

* Thormar H, et al; Inactivation of enveloped viruses and killing of cells by fatty acids and monoglycerides. Antimicrob Agents Chemother. 1987;31(1):27-31. doi:10.1128/AAC.31.1.27.

Zap-H™ comprises such fatty acids that disrupt viral membranes. Furthermore, in-vitro (i.e., lab tests) testing has shown rapid killing of viral particles by Zap-H™. In this way, Zap-H™ kills HSV viral particles directly by disrupting their outer envelope. Additionally, viral membrane disruption results in exposing hidden viral markers that the immune system can now target, allowing the immune system to eradicate the herpesvirus.

Although numerous fatty acids/ oils can kill viruses, the combination of ingredients in Zap-H™ significantly enhances, i.e., synergizes, such viral killing. As previously noted, this combination mimics how mother's milk ingredients provide antimicrobial protection. Our laboratory studies demonstrate that the combination of ingredients in Zap-H™ significantly enhances, i.e., synergizes, such viral killing more profoundly than does any single ingredient used alone. Our hospital clinical study and human testing results are consistent with our laboratory testing, confirming that the combination of ingredients in Zap-H™ dramatically improves the impact on cold sore healing beyond using any of the ingredients alone.

While laboratory studies show viral envelope disruption and a viral killing feature by fatty acids, any clinical effect has not been evaluated by the FDA. However, the rapid in-vitro viral envelope disruption and viral killing correlates with a rapid in-vivo effect (i.e. demonstrated with a double-blind, hospital clinical study showing a significant reduction in time for symptoms to disappear). In other words, our laboratory research testing correlates highly with results obtained with the clinical use of Zap-H™.

Effective even at 5 days post onset of symptoms

Our clinical experience further shows that individuals using Zap-H™ anecdotally note that it is effective in reducing symptoms and duration even if treatment application begins after the blisters have formed, i.e., up to 5 days after onset of a cold sore (see also below on biofilm) This is a benefit over viral entry blocking agents and prescription antiviral medications, which need to be started within 2 days of the onset of a cold sore, being ineffective once blisters form. Although beneficial results at 2-5 days after onset of a sore have been noted with Zap-H™, such results may vary between individuals.

Generalized Antiviral Effect

Zap-H™ has also shown antiviral efficacy against other viruses that were tested in the lab. These pertain not only to herpesvirus, but also coronavirus, RSV (respiratory syncytial virus), influenza and Mpox viruses. The formulations need to be altered for specific viruses for best results - the same formula is not optimal for every virus. We do not advocate that the Zap-H™ formulation should be used to mitigate symptoms for these other viruses, but the lab results further confirm the general antiviral features of Zap-H™ ingredients.

Zap-H™ & Skin Absorption

A benefit for Zap-H™ is rapid skin absorption. Moreover, when an antiviral formulation is applied topically, to be effective, it needs to penetrate the skin such that the active ingredients can reach the viral particles which are buried under the skin, and potentially within biofilm. Zap-H™ comprises a water-based formulation with rapid skin penetration, which is a vital component of its clinical efficacy. Furthermore, a formulation that absorbs well does not leave a visible or irritating residue on the skin/lip.

When we tested numerous over-the-counter (OTC) products, it was noted that most did not have good skin absorption properties. Docosanol, for example, has poor skin permeation properties. In fact, in the 'Product Monograph' of a Viral Entry Blocking Agent comprising a docosanol 10% cream, on November 26, 2013, it specifically states "Dermal and gastrointestinal absorption of docosanol.....is limited.....".

If a composition does not absorb through the skin, then one can imagine that there is limited ability for such a product to target a virus, which is lodged deep underneath the skin surface. Zap-H™, on the other hand, absorbs quickly, typically within 5-10 minutes. This is due to the presence of skin permeation enhancers in the Zap-H™ formula. Such rapid penetration through the skin and into the local tissues allows for the ingredients to reach the cells. Any viral particles that are either ready to enter a host cell, or those newly formed viral particles that have exited the cells can be targeted by the absorbed Zap-H™, which will disrupt the viral envelope, allowing the immune system to eradicate the virus.

Zap-H™ & Biofilm

An additional benefit for Zap-H™ pertains to biofilm. Biofilm is a complex extracellular matrix that is formed by microorganisms which protects them from substances in their local micro-environment, and this includes antibiotics, antiviral agents, and some antiseptic agents. Biofilm also protects viruses that may be hidden within such bacterial or fungal biofilms.

Zap-H™ cream was initially developed as an antibacterial biofilm disrupting technology, before it was found to aid the body's antiviral effectiveness. The Zap-H™ formulation breaks down biofilm in multiple types of microorganisms. In-vitro lab testing at an independent top microbiology testing center demonstrates effects against mature biofilm organisms, including Gram positive Staph. aureus and Enterococcus; Gram negative Pseudomonas aeruginosa, E. coli, and Klebsiella pneumonia; and Candida fungal biofilm.

When open sores develop, bacteria infiltrate such open wounds, and form biofilm as a manner by which to protect themselves. Bacteria are known to reside within biofilm in the eschar (i.e., scab) above a wound bed, such as a scabbed cold sore lesion. Viruses are known to lodge within bacterial and fungal biofilms. In this respect, after a cold sore blister breaks and the scab forms the herpesvirus can exist in the bacterial biofilm of the cold sore eschar. Because Zap-H™ disrupts biofilm, this is yet an additional benefit as it can target viruses that may be present within biofilm located on open sores. Moreover, if one could break down biofilm (such as with Zap-H™), it would expose the encased viral particles, rendering them susceptible to topical viral envelope-disrupting agents, such as Zap-H™, and the body's immune response. In other words, Zap-H™ does both – it first disrupts the biofilm to expose the viral particles and subsequently dissolves the viral membranes thus allowing for the killing of the now-exposed viral particles by the immune system. This is correlated clinically by individuals where treatment of cold sores with Zap-H™ was started up to 5 days from symptom onset. At this stage the outbreak formed an eschar (i.e., scab). Nonetheless, subjects reported that their symptoms were resolved more quickly with Zap-H™ application, even at this relatively late stage of treatment, as compared to an untreated cold sore scabbed lesion. (This evidence is anecdotal and individual results may vary.)

GENITAL HERPES

The genital herpesvirus (HSV2) is structurally very similar to the cold sore HSV1 virus particle. The viral envelopes are similar, as both are formed from the host cell wall. In this respect, because Zap-H™ targets the viral envelope, it theoretically would have effectiveness against the genital HSV2 viral envelope. Clinical testing for genital herpes has not yet been performed. At this time, we are not able to recommend Zap-H™ for use on HSV2 or genital herpes sores. The information provided herein is for healthcare professionals.

SHINGLES

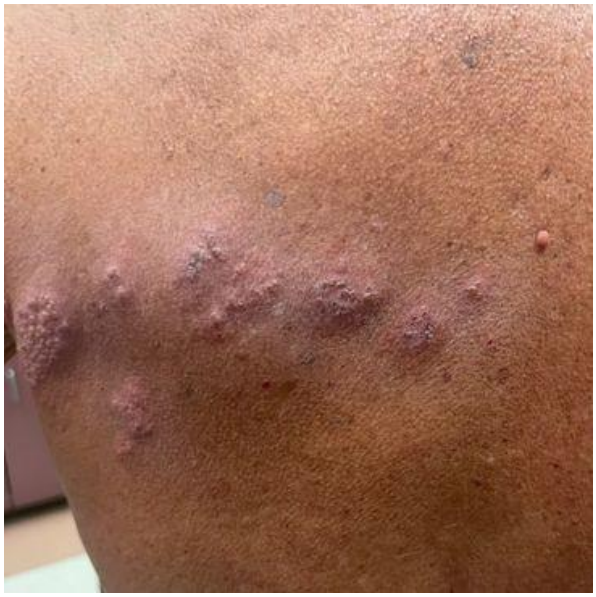
Shingles rash is the reactivation of the chicken pox herpesvirus (Varicella Zoster, or Herpes Zoster - HZ) infection in adults. It can be very painful and debilitating. Zap-H™ has not been formally tested for shingles, however, because shingles is caused by a similar herpesvirus, with a similar viral envelope, anecdotal reports indicate that it may be effective in relieving pain symptoms of the shingles rash and reducing duration of the rash. Because no formal testing has been done for shingles, at this time we cannot recommend the use of Zap-H™ for application on shingles sores. This information is provided for healthcare professionals.

#1 SHINGLES (CASE STUDY) BEFORE ZAP-H™
PHOTO: 68 year old, healthy male, unvaccinated for shingles. Day 4 of shingles outbreak. Symptoms of pain, itch and tingling.

#2 SHINGLES (CASE STUDY) AFTER ZAP-H™
PHOTO: Day 6, after applying Zap-H™ on Day 4, 5 and 6. Painful symptoms were relieved more rapidly than the typical duration of 3-5 weeks.

Note. This is only one example, and it does not prove that Zap-H™ will have similar results for other subjects. We show this to highlight that Zap-H™ ingredients have a unique ability to potentially help the body's immune system to better deal with a viral skin infection. Zap-H™ does not cure any disease and has not been tested or approved by the FDA for use in treating symptoms associated with a shingles outbreak. This information is provided for healthcare professionals.

#1



#2