VIROPLAZIN

Chemical name of Viroplazin

Supramolecular complex of (2R)-2-phenyl-2-[(2R,3R,4S,5S,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxyacetonitrile and disodium thiosulfate* 5H2O

Essence of the manufacturing process

The product is made through a multi-step process.
Step 1: preparation of the mandelonitrile glycoside in a purified, enzyme-free form.
Step 2: pre-complexation of the glycoside with sodium thiosulfate within a strictly maintained, narrow thermodynamic range at 25–40 °C. Depending on temperature, complexation takes between 10 minutes and 2 hours of incubation.

Complexation can proceed in two different ways: a **solid-state reaction** or **solution-phase complexation**. The powder formulation is produced by the solid-state route. The final product is a **supramolecular complex** that is stable and can be stored indefinitely, provided the upper limit of the thermal/thermodynamic range is not exceeded for prolonged periods during storage.

III. General overview

Viroplazin is a stabilized molecular complex that acts by **enhancing the efficiency of the innate immune system**, i.e., via self regulating redox-buffering mechanism and production of hypothiocyanate . The compound enters the body as a **prodrug (precursor molecule)** and becomes biologically active through **enzymatic activation**. The active molecules—**thiocyanate, hypothiocyanite, and benzaldehyde**—are generated within the body with the participation of the specific native enzyme system of the mucus membranes and the immune cells.

This enzymatic activation occurs **locally** in virus- or bacterium-infected tissues, achieving high therapeutic concentrations at the site of infection while maintaining **very low systemic levels**. Owing to this pharmacodynamic profile, the drug combines high efficacy with **very low toxicity**; therefore, its **therapeutic index (TI = TD50 / ED50)** is high—in the case of Viroplazin **greater than 1000:1**.

IV. Mechanism of Action

Understanding the mode of action of **Viroplazin** requires a brief overview of the **pathomechanism of viral infections**.

1. Viral Infection Dynamics

At the onset of infection, viruses enter a phase of **exponential replication**. Viral particles invade host cells, hijack their metabolic machinery to synthesize viral DNA/RNA and structural proteins, and assemble thousands to millions of progeny virions. Eventually, the infected cell undergoes **pyroptosis /apoptosis** or lysis or become senescent but before this degradation occur releasing newly formed virions to infect adjacent cells.

During recovery, **pluripotent stem cells** and tissue-resident progenitors restore cellular integrity and heal damaged tissue. From this simplified model, it becomes evident that **effective antiviral therapy requires a dual approach**:

1. **Inhibiting viral replication within infected cells**

2. **Neutralizing virions already released into the extracellular environment**

2. Pyroptosis: Harnessing the Body's Innate Defense

One of the fastest and most efficient strategies to halt viral replication in infected cells is the induction of **inflammatory programmed cell death**, known as **pyroptosis** *(refs. 10, 11)*.

- **Role of pyroptosis:**
  Once a cell is infected, its ultimate fate is death. However, without intervention, the cell can release millions of virions before succumbing, perpetuating the infection.

- **Mechanism:**
  Pyroptosis is triggered by viral RNA/DNA or bacterial components, activating **caspase-1**, **inflammasomes**, and **interleukin complexes**. These processes rapidly terminate the infected cell **before virion release**.

- **Scientific importance:**
  Pyroptosis remains a rapidly evolving area of immunology, but current findings indicate that Viroplazin activates metabolites critical to initiating this pathway *(refs. 7, 8, 11)*.

This mechanism serves as a **frontline containment strategy**, shutting down infected cells before systemic spread occurs. Unfortunately, in many viral diseases, the **adaptive immune response**—T-cell activation, antibody production, and infected-cell clearance—occurs too slowly, contributing to severe illness or fatal outcomes.

3. Viroplazin: Amplifying Early Innate Immunity via Host-Directed Pathways

Viroplazin initiates a **rapid, host-directed immunomodulatory response** by enhancing early innate immune mechanisms **prior to the activation of adaptive immunity**. Unlike conventional antivirals that target virus-specific enzymes, Viroplazin modulates the host's own **redox-based defense systems** and **innate immune cascades**, providing an accelerated response during the **critical early window of viral infection**.

3.1. Rapid Mobilization of Innate Immune Cells

Experimental data demonstrate that within **two hours** following a **single 5 mg/kg injection dose**, Viroplazin induces a **20% to 150% increase** in circulating **neutrophils** and **lymphocytes**. Remarkably, this effect persists even in subjects exhibiting **immune exhaustion**—a pathological state commonly associated with impaired antiviral responsiveness. This rapid leukocyte mobilization suggests **upstream activation of innate immune pathways**, effectively "resetting" host defense capabilities.

3.2. Inflammasome and Cytokine Pathway Activation

The early rise in immune cell counts is frequently accompanied by a **transient, self-limited elevation of body temperature**, reflecting an orchestrated inflammatory response. Mechanistic analyses strongly implicate activation of the **NLRP3 inflammasome**, leading to **Caspase-1–mediated cleavage** of precursor cytokines and subsequent release of **interleukin-1β (IL-1β)** and **interleukin-18 (IL-18)**.

This cascade plays a **pivotal role** in amplifying antiviral defense by:

- Enhancing **innate immune cell recruitment** to infected tissues
- Accelerating the activation of **natural killer (NK) cells**
- Facilitating cross-talk with adaptive immune pathways to optimize long-term immunity

3.3. Integration with the Lactoperoxidase System and $OSCN^-$ Production

Beyond cytokine activation, Viroplazin acts as a **potent modulator of the lactoperoxidase system**—a critical mucosal defense mechanism. By stimulating endogenous pathways that convert thiocyanate (SCN^-) into **hypothiocyanite ($OSCN^-$)**, Viroplazin triggers the production of a **highly reactive, broad-spectrum antiviral oxidant**.

$OSCN^-$ exerts **direct virucidal effects** by:

- Disrupting viral envelope integrity

- Oxidizing essential cysteine residues in viral proteins
- Inhibiting viral replication independently of classical enzymatic inhibition

3.4. Clinical Implications

This **dual mechanism**—innate immune activation plus direct antiviral activity—positions Viroplazin as a **first-in-class therapeutic** capable of providing a **critical advantage** during the earliest stages of infection. By bridging innate and adaptive immunity, Viroplazin may not only **enhance viral clearance** but also **support the development of natural, variant-specific immunity**—a feature of particular relevance for emerging and rapidly mutating viral pathogens.

Key Highlights

- **Fast-acting immune priming:** 20–150% increase in innate immune cells within 2 h
- **Broad innate pathway activation:** NLRP3 → Caspase-1 → IL-1β / IL-18
- **Direct virucidal activity:** Hypothiocyanite-mediated redox mechanism
- **Potential cross-species benefit:** Mechanistic independence from viral genotype

4. Activation Mechanism: Inflammation-Triggered Precision

Viroplazin activation is a **multi-step, self-regulating process** initiated **only at sites of inflammation**, which provides both specificity and safety.

1. **Triggering event** – Local inflammation caused by viral or bacterial infection.
2. **Enzymatic activation** – Lysosomal hydrolyses released by immune cells in inflamed tissue catalyze the initial conversion of Viroplazin *(refs. 5, 6)*.
3. **Specificity** – This localized activation ensures that:
    - **Healthy tissues remain unaffected.**
    - No off-target antiviral activity occurs in uninfected cells.
    - Viral replication in artificial cell culture models remains unaffected unless inflammatory pathways are engaged.

This phenomenon has been **experimentally confirmed** and highlights Viroplazin's role in **enhancing, rather than bypassing, natural host defenses**.

5. The Thiocyanate–Peroxidase Pathway: Local Production of a Natural Virucid

A central aspect of Viroplazin's action involves the **endogenous thiocyanate-peroxidase defense system**:

- **Step 1:** Activation of mitochondrial **sulfurtransferases**, including **rhodanese enzymes**.
- **Step 2:** Formation of **thiocyanate compounds**.
- **Step 3:** In the presence of **lactoperoxidase** or **myeloperoxidase** and **hydrogen peroxide**, these thiocyanates are converted into **hypothiocyanite ($OSCN^-$)** *(ref. 15)*.
- **Step 4:** $OSCN^-$ acts as a **potent, broad-spectrum virucid**, disrupting viral envelopes and capsids.

Viroplazin amplifies this pathway by **increasing the local production of hypothiocyanite** at the precise site and time where it is most needed *(refs. 1–6, 9)*.

6. Additional Antibacterial Synergy

Recent studies suggest that **mammalian thioredoxin reductase (TrxR)** rapidly detoxifies $OSCN^-$, protecting redox-sensitive host cell components. In contrast, many bacteria lack an efficient equivalent enzyme, making them **highly susceptible** to $OSCN^-$-mediated damage *(ref. 16)*.

As a result, Viroplazin may also demonstrate **adjunct antibacterial properties**, particularly against opportunistic infections accompanying viral disease how ever do not fully substitute antibiotics.

7. Safety Profile

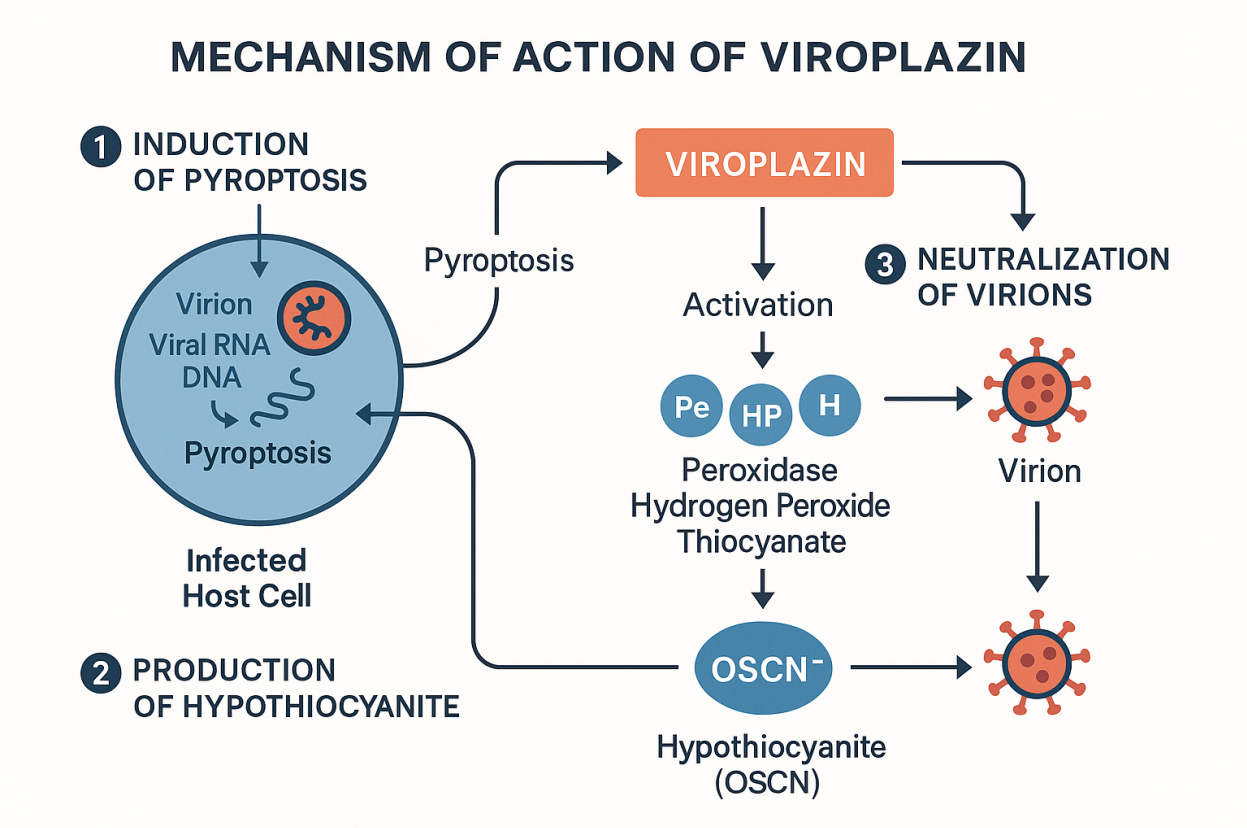
Over **10 years of veterinary testing and clinical use** have demonstrated an **exceptional safety record**:

- **Prodrug selectivity** – Activation occurs **only in inflamed tissue**.
- **No systemic toxicity** – Viroplazin remains inactive in healthy cells.
- **Physiological compatibility** – The compound enhances **existing endogenous pathways** rather than introducing artificial mechanisms.
- **Absence of off-target effects** – Unlike many marketed antivirals, Viroplazin does **not** interfere with essential metabolic or signaling pathways at therapeutic doses.

This safety profile, combined with **broad-spectrum efficacy**, distinguishes Viroplazin from conventional antivirals that rely on **direct enzyme inhibition** and are often associated with drug resistance or cytotoxicity.

Summary

Viroplazin represents a **novel therapeutic approach**: rather than targeting viral enzymes directly, it **activates and amplifies natural host defense systems**. By enhancing pyroptosis and boosting local production of **hypothiocyanite**, Viroplazin achieves rapid viral neutralization while maintaining an excellent safety margin.



This unique mechanism explains:

- Its **broad antiviral spectrum**
- Its **synergy with immune function**
- Its **lack of observed adverse effects** after a decade of veterinary use

V. Dosage and Administration

1. Effective Dose Determination

Clinical titration studies have demonstrated a **dose-dependent therapeutic response** for **Viroplazin**:

- Doses **2 mg/kg/ body weight** show **suboptimal antiviral activity** and delayed clinical response.
- Doses **above 15 mg/kg** do **not** provide additional therapeutic benefit in terms of recovery speed or overall efficacy.

These findings establish an **optimal therapeutic range** of **3–6 mg/kg body weight**, depending on disease severity and clinical presentation.

2. Recommended Dosing Guidelines

Clinical Context	Dosage	Frequency	Notes
Minimum effective dose	**3 mg/kg**	2-3 x daily	Lowest dose with measurable efficacy
Typical medium dose	**5 mg/kg**	2-3 x daily	Recommended for mild to moderate strong infections
Severe infections	**6 mg/kg**	3-5x daily	For high viral burden or systemic

3. Duration of Therapy

- **Clinical improvement** is typically observed within **1–3 days** of initiating treatment.
- **Treatment must continue for a minimum of 5 days**, even if symptoms resolve earlier, to minimize the risk of **viral resurgence** or **secondary flare-ups**. If flare-up occurs after the initial treatment was stoped the medication can be restarted .
- **If Viroplazin do not handle the infection it is most likely bacterial origin or the symptoms are continued because of secondary bacterial infection occurred and it is necessary to administer effective antibiotic !**

4. Co-Administration Considerations

Due to Viroplazin's **mechanism of action**, concurrent administration of **high-dose antioxidants** is **not recommended**. Substances such as:

- **Vitamin C**
- **Vitamin E**

- **Polyunsaturated fatty acids (PUFAs)**
- Other strong reducing agents

…may **neutralize hypothiocyanite ($OSCN^-$)**, the **endogenous virucidal compound** generated during Viroplazin activation, potentially reducing therapeutic efficacy.

5. Clinical Implications

- Optimal dosing maximizes **intracellular $OSCN^-$ generation** and **pyroptosis-mediated viral clearance**.
- Dose escalation beyond **10 mg/kg** is generally unnecessary, as it **does not enhance efficacy** but may increase treatment cost.
- Treatment duration should always consider **viral kinetics**, **disease severity**, and **host immune response**.