

Molecular Iodine: A Novel Broad-Spectrum Antiviral Agent against SARS-Cov-2

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Abstract

Corona viruses are a group of RNA viruses that cause respiratory infection in mammals and birds. The ongoing COVID-19 pandemic has heightened the battle between humans and viruses. At this time, it is critical for everyone to take precautionary measures in order to avoid becoming infected. Physical barriers, such as masks, PPE kits, and face-shields, as well as maintaining social distance, are recommended. Chemical barriers, such as hand sanitizers, sprays, and hand-washes, are also recommended along with vaccinations. Another lesser-known but well-proven method for combating Covid is to use Iodine as an antiviral agent. Iodine has broad-spectrum disinfectant properties. According to laboratory studies, iodine exposure inactivates the SARS virus within few minutes. Iodine can be taken in the form of Povidone-iodine (PVP-I) gargles or Iodine V (available in the form of Essential Iodine Drops) or the use of molecular iodine (I₂) in the form of lotion (I₂ Cure). Iodine acts on viruses by damaging viral surface proteins and lipid coating. Free iodine can cause irreversible damage to the virus by degrading viral nucleoproteins, oxidising nucleic acids, and disrupting metabolic pathways. Furthermore, free iodine is an anti-inflammatory agent during viral infections because it scavenges free radicals. Iodine's above action results in the inactivation of the cell/viral particle. Although the use of iodine seems as a promising method of inactivating viruses, the effects of long-term exposure to Iodine is not fully evaluated.

The purpose of this paper is to understand a relatively unknown but well-proven mode of disinfection, namely the use of molecular iodine, against Corona virus.

Keywords: COVID, Molecular Iodine, Antiviral agent, Antimicrobial Agent, SARS-CoV-2

INTRODUCTION

Corona viruses are single-stranded RNA viruses that belong to the Orthocoronavirinae subfamily. The effects of this virus family range from a common cold to serious respiratory health risks. COVID-19 is caused by the SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus-2) strain. In November 2019, the first COVID patient was located in Wuhan, China. Since then, the virus has replicated and spread at breakneck speed, resulting in a global pandemic. The Corona Virus is primarily transmitted by small droplets from the nose or mouth of infected individuals. These viral particle-containing droplets can spread through sneezing, coughing, or surface contact. Because of the lower stability of RNA as genetic material and the increased replication cycles during the pandemic, SARS-CoV-2 has quickly undergone mutations, resulting in the formation of variants. There are currently five known variants of the SARS-CoV-2 virus: alpha,

beta, gamma, delta and the newly emerged omicron variant.

As responsible humans, it is our sole duty to take precautions to avoid becoming infected or possibly transmitting infection. We should maintain social distance, wear masks, get vaccinated, and wash our hands with soap or sanitizer on a frequent basis.

[8]

Iodine a Novel Broad-Spectrum Antimicrobial Agent

Natural elemental iodine is a widely used antiseptic agent since 1800s. [3] It is the least-heaviest, stable halogen. Iodine, as a small molecule can penetrate the cell membranes and cell-walls and can oxidise the cell components like proteins, nucleic acids and fatty acids resulting in death of the microorganism. It has broad antimicrobial activity not only against gram positive and negative bacteria, but also against antibiotic and antiseptic resistant strains, as well as some bacterial spores. It is also effective against fungi,

protozoa, and a variety of enveloped and non-enveloped viruses. ^[10]

Iodine has the lowest halogen reactivity, making it the most biologically compatible. ^[5] Like all halogens, it's generally found in nature in compounded or ionized forms. Iodine is stabilised by addition of iodophors. Iodophors are iodine - containing complexes, which act as a carrier or slow releasing agent. It serves as a reservoir of "free" active iodine. ^[12]

Bearing this in mind, researchers attempted to use molecular iodine as an antiviral agent during the recent Corona pandemic. This was prompted by the use of various iodine-based compositions to eliminate the Covid-19 virus. Thus, research and laboratory work have been conducted all over the world to test the activity of Iodine against SARS-CoV-2 virus. ^[4]

Our literature review mainly focuses on three sources of Molecular Iodine

- Povidone - Iodine (PVP-I)
- Iodine-V (Essential Iodine Drops-EID)
- I2 cure lotion

1. Povidone Iodine

Like all halogens, iodine is generally not found in nature unless compounded or ionized ^[5]. Povidone-iodine (PVP-I), a complex of the polymer polyvinylpyrrolidone and iodine, is a water-soluble powder containing 10% iodine. PVP forms a polymeric complex with elemental iodine that improves tolerability, stability and solubility in water. Free iodine is delivered from the PVP-I complex where it is carried in a less-irritating form. It is this delivery of free iodine that provides for the rapid microbicidal activity of PVP-I. ^[2]

Iodine enters bacteria quickly and targets important protein groups (cytosine and methionine), nucleotides, and fatty acids. In enveloped viruses such as SARS-CoV-2 iodine destabilises viral envelope, thus damaging the viral surface proteins. PVP-I also interacts with unsaturated fatty acids and amino acids within the cell, impairing protein synthesis. Free iodine can degrade viral nucleoproteins, oxidise nucleic acids, and disrupt metabolic pathways, all of which can cause irreversible damage to the virus. In addition, free iodine scavenges free radicals, making it an anti-inflammatory agent during viral infections ^[11, 15]

An experiment conducted on viruses which included both enveloped and non-

enveloped viruses (like adeno-, mumps, rota-, polio- (types 1 and 3), coxsackie-, rhino-, herpes simplex, rubella, measles, influenza and human immunodeficiency viruses) in Japan, found that PVP-I in the form of solutions, gargles and creams, could effectively inactivate all the tested virus species within a short period of time^[9] In another experiment, when viruses were treated with two formulations of PVP-I, Aqueous and Liposomal PVP-I, both showed equivalent activity. Necrosis occurred in cells treated with aqueous 0.08 -0.32% PVP-I solutions, whereas apoptosis occurred in cells treated with same concentrations of liposomal PVP-I. The use of Liposomal PVP-I for topical treatment to treat infections of the upper respiratory tract was found to be more favourable in this investigation.^[15]

Povidone Iodine at 10% concentration was found to be a better viricidal agent with a wider spectrum than 70% ethanol. When applied to healthy skin, PVP-I solution were found to be active for 12-14hours. Under in vitro conditions, the effect of Povidone can be seen within 30 seconds. A recent study which tested the action of PVP-I under different concentrations (4 and 7.5%) and different exposure times of 0.25, 0.5, 2.5 and 5 minutes shows positive viricidal activity.^[10]

In a recent laboratory study, SARS-CoV-2 was promptly inactivated by povidone-iodine nasal antiseptics at concentrations as low as 0.5 percent after only 15 seconds of contact. PVP-I intranasal use has been shown to be safe at doses of 1.25 percent and below, suggesting that it could be used as a supplement to PPE in preventing viral transmission. Each of the nasal antiseptics examined had no cytotoxic effects on cells.^[4] A clinical study compared the use of PVP-I vs. essential oils and tap water. The results suggestive that all the Stage I- COVID patients who had used beta dine (PVP-I) showed early viral clearance on day 6.^[6]

In another randomised clinical trial on highly positive COVID outpatients, all patients except 1 had negative viral titre by day 3. "The intervention consisted of four successive mouthwashes and gargles with 25 ml of 1% aqueous PI solution, followed by one 2.5- mL nasal pulverisation of the same solution into each nostril using an intranasal mucosal atomization device connected to a 5-mL syringe while sniffing and one application on each nasal mucosa of a dab of 10% PI ointment followed by a massage of the nostril to help spread the ointment." The RT-PCR tests were taken

at least 3 hours after the above mentioned procedure.^[5]

The above data suggests that Iodine, in the form of PVP-I is capable of inactivating the novel Corona Virus, thus is a possible precautionary method which can be used to reduce viral load in the nasopharyngeal region, throat and prevent shed of viral load.

2. Iodine-V

Iodine-V is a novel complex derivative of Fulvic acid in a clathrate complex by a molecule of elemental iodine (I₂). In a recent stand-alone laboratory work conducted, SARS-CoV-2 was subjected to viricidal action by EID (Essential Iodine Drops). The results showed that 99% of SARS-CoV-2 viruses were inactivated after 60 and 90 seconds. Similar results were observed with Povidone-Iodine (PVP-I). The study suggests that Iodine-V being excipient free, will have greater in vivo stability and potency as compared to PVP-I.

As a result, when used as a nasal or oral antiseptic, Iodine-V has the potential to remove or inactivate shed virus from respiratory secretions of known or suspected patients. More research is needed

into the use of Iodine-V and its improved potential against Covid-19 virus.^[2]

3. I2Cure- Molecular iodine lotion

I2 Cure is a Delhi and Gurgaon-based company. It has created a product called I2Cure Bio Shield TM Lotion, which claims to be a Bio Shield that aids in Covid defence. The formula contains molecular iodine stabilised at 1500 ppm in 100% vegetable grade glycerine. This lotion has a non-drying glycerine base and is a non-staining emollient iodine-based antiseptic lotion. It employs the iodine mechanism to combat pathogens. Slow release of molecular iodine from the skin forms an antimicrobial vapour shield around the epidermal surface of the skin.

Unlike other alcohol-based sanitizers that only provide short-term antimicrobial activity, I2Cure claims to provide 12-hour protection against not only Corona virus but also all other types of pathogens such as other viruses, bacteria, and fungi with just two tiny drops. Iodine has been tested and proven to be the most effective non-toxic biocide. There are no molecular iodine-resistant pathogens known. Further being alcohol-free, it is considered extremely safe to use in high heat industrial settings, commercial areas, as well as at religious sites.^[7]

The three major iodine based anti-covid viral agents have been tested as human trials as well. However, it is established that mode of action on viral protein remains same. Keeping in view of the cost and simplicity of preparation, iodine can be a hope of widespread antiviral agent in future.

Side Effects of Over Exposure to Iodine

Although Povidone-iodine (PVP-I) and Iodine-V are typically safe, some persons may develop negative effects.

- Thyroid impairment caused by PVP-I has been documented.
- High-concentration or high-amount PVP-I consumption might cause liver toxicity or acute renal injury, as well as metabolic acidosis, hyperthyroidism and hypothyroidism.

Although the side effects are linked to thyroid glands and hormone functioning, much information about the extent of damage and rate of reversibility is still awaited. As a result, the use of iodine-based nasal spray, gargles, and other forms without side effects has yet to be clinically proven. To further demonstrate its antiviral activity, a careful large-scale trial-based experiment involving Covid patients is required.^[13, 14]

CONCLUSION

Covid-19 is a global pandemic that has claimed the lives of millions of people. Iodine can be used in the form of gargles, nasal spray, nasal drops or Bio Shield Lotion. Iodine, in the form of 0.5 percent PVP-I and Iodine-V, has been demonstrated to inactivate the SARS-CoV-2 virus in under 30 seconds. Although a study found that all Covid-causing viruses are inactivated within 15 seconds of contact, it is fair to assume that all Covid-causing viruses are inactivated within one minute. Furthermore, iodine's influence lasts longer than its initial activity. Iodine penetrates the skin, is absorbed in 30 seconds, and then resurfaces as fumes, continuing to operate as an antimicrobial agent. It works well against viruses, bacteria, fungus, protozoa, and even spores. There are no organisms that have developed resistance to iodine, according to studies. Cell cytotoxicity was also found to be low in studies.

Iodine is an excellent antimicrobial agent, and its cost-effectiveness and low morbidity make it an excellent weapon against SARS-CoV-2.

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