

## Molecular Iodine ( $I_2$ ): It's Occurrence, uses and safety profile

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**ABSTRACT:** In this article we review that Iodine an element belongs to halogen family found abundantly in nature is required by the body to make thyroid hormones triiodothyronine (T3) and thyroxin (T4) for the development. Deficiency of Iodine in the body causes dry, flaky skin and hair fall. The Recommended Dietary Allowance (RDA) of Iodine in India for adult men and women is 65-150 µg/day. Molecular iodine ( $I_2$ ), an active species of Iodine, which is found in different seaweed and algae, is a broad-spectrum antimicrobial. It is preferred over other species of Iodine i.e., Iodide ( $I^-$ ), iodate ( $IO_3^-$ ), triiodide ( $I_3^-$ ), polyiodide ( $I_5^-$ ) because it does not stain, has no odour, no side effects and active as antimicrobial. Molecular iodine ( $I_2$ ) is used as a skin antiseptic, in wounds, acne & dandruff and also used for air & water disinfection, in endometritis & mastalgia. Molecular iodine ( $I_2$ ) is completely safe for use and non-toxic in nature. FDA has categorized molecular iodine ( $I_2$ ) under Category D& due to its safety profile, molecular iodine can be utilized in many areas as therapeutic & curative approach for short term or long-term therapies.

**KEYWORDS:** Molecular iodine ( $I_2$ ), antimicrobial, antiseptic, disinfection, Covid-19, seaweed.

### I. INTRODUCTION

Iodine is a crucial micronutrient which is required at all stages of life, out of that early childhood being the most critical phases of requirement. Iodine is mostly concentrated in the thyroid gland. A healthy adult body accommodates approximately 10-20 mg of iodine, out of which 70-80% is stored in thyroid gland. Iodine is used by the body to make thyroid hormones triiodothyronine (T3) and thyroxin (T4) which controls the body's metabolism, bone and brain development

during pregnancy and infancy. Iodine helps in regeneration of skin cells, regulates sweat glands and hydrates skin cells. Iodine deficiency can cause dry, flaky skin, sensitivity to cold and may prevent hair follicles from regenerating [1]. In India, the Recommended Dietary Allowance (RDA) of Iodine is 75-150 µg/day for adult men and women. The median intake of iodine in United States for men is approximately 240-300 µg/day and 190-210 µg/day for women [1]. 2000-3000 mg of iodine orally is estimated to be lethal to humans, but survival has been reported after ingestion of 10,000 mg. The maximal safe dietary dose of iodine is considered to be 500-1000 µg/day in adults (8-16 µg/kg per day based on 60 kg) [2].

Iodine exists in many species like iodate ( $IO_3^-$ ), Iodide ( $I^-$ ), triiodide ( $I_3^-$ ), polyiodide ( $I_5^-$ ) and Molecular iodine ( $I_2$ ). Molecular Iodine ( $I_2$ ) consists of two iodine atoms covalently bound together. It exists as shiny violet-black crystals with a metallic lustre in nature. Molecular Iodine ( $I_2$ ) is also known as elemental iodine. It sublimes at room temperature and emits violet-purple vapour when its concentration builds up in a confined space (See Table 1) [3].

Molecular iodine ( $I_2$ ) is the only species of iodine which represents some therapeutic efficacy in many applied areas. It is found to be a broad-spectrum antimicrobial which exerts its effects on multiple species [4]. Molecular iodine ( $I_2$ ) was first discovered by Bernard Courtois in November, 1811 while replacing wood ashes as the raw material for soda by the ashes of brown seaweeds which resulted in the emission of previously unobserved violet vapor i.e., molecular iodine ( $I_2$ ). This discovery was further studied & confirmed by Davy and Joseph Louis Gay-Lussac [5].

Table 1- Physical & chemical properties of Molecular iodine ( $I_2$ )

CHEMICAL IDENTIFICATION
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Molecular formula	I <sub>2</sub>
Synonyms	Molecular iodine, diatomic iodine, free iodine
<b>PHYSICAL PROPERTIES</b>	
Physical description	Violet-black crystals with metallic lusture.
Molecular weight	253.8
Boiling point	183°C
Melting point	185°C (sublimes)
Specific gravity/ density	4.96gm/ml

Table 1- represents the physical & chemical properties of molecular iodine (I<sub>2</sub>), physical properties as well as chemical properties.

## II. OCCURENCE

Oceans/seawater is the largest reservoir of molecular Iodine (I<sub>2</sub>), holding about 34.5 million tons. But the concentrations are so low averaging between 50 to 60 parts per billion (ppb). Commercially molecular Iodine (I<sub>2</sub>) is extracted from seaweed in large quantities. From many species of seaweed, the main reservoirs of molecular iodine are brown and red algae.

Molecular iodine (I<sub>2</sub>), in volatile form is released from wet algal surface at very high flux rates by the process of "Iodovolatilization" i.e., direct reaction of ozone with the accumulated iodide. The main stored reserves of molecular iodine in the world are in brines or Caliche ore which are mainly in Japan, Chile, USA, Turkmenistan, Azerbaijan and Indonesia [5].(See Table 2) [6].

**Table 2- Sources of Molecular iodine (I<sub>2</sub>)& its presence**

SOURCE	I <sub>2</sub> CONTENT	OCCURRENCE
<u>Brown seaweed</u> Laminaria japonica (Kombu kelp)	2984 mcg/gm	Between seas of China, Korea & Japan, rocky French Atlanta coasts.
<u>Brown seaweed</u> Undariapinnatifida (Wakame)	66 mcg/gm	Native to cold, coasts of northwest Pacific Ocean. From Russia to coasts of Japan, Korea, China & Hong-Kong
<u>Red algae</u> Porphyraumbilicalis (Nori)	16-43 mcg/gm	Japan, Tokyo

Table 2- represents the molecular Iodine (I<sub>2</sub>) content in different species of seaweed i.e., brown and red algae. Table also shows the abundance of molecular Iodine (I<sub>2</sub>) in different countries across the world.

## III. SOLUBILITY OF MOLECULAR IODINE (I<sub>2</sub>)

Molecular iodine (I<sub>2</sub>) is practically insoluble in water but is very soluble in aqueous solutions of iodides forming the water-soluble ion triiodide (I<sub>3</sub><sup>-</sup>) [7]. Molecular iodine (I<sub>2</sub>) is soluble in

non-aqueous media, organic solvents (carbon tetrachloride, diethyl ether, chloroform, etc.) giving a violet-brown colour solution. There is no degradation of molecular iodine in non-aqueous media reported so far [8]. (See Table 3) [5].

**Table 3- Solubility of Molecular iodine (I<sub>2</sub>)**

SOLUBILITY	
SOLVENT	RATIO (I <sub>2</sub> : SOLVENT)
AQUEOUS	

Water	1:3000
NON-AQUEOUS	
Alcohol	1:13
Glycerol	1:80
Carbon disulphide	1:4
Chloroform	1:30

Table 3- represents the solubility of molecular iodine ( $I_2$ ) in aqueous and non-aqueous media in different ratios of  $I_2$  and solvent. It depicts the solubility concentration of molecular iodine ( $I_2$ ) parts per ratio (ppr).

#### IV. MOLECULAR IODINE ( $I_2$ ) AS ANTIMICROBIAL

Molecular iodine ( $I_2$ ) is a broad-spectrum antimicrobial; it does not stain, has no odour and has bactericidal, fungicidal, tuberculocidal, viricidal, and sporicidal activity in acidic and neutral medium. Whereas, other species of Iodine i.e., Iodide ( $I^-$ ), iodate ( $IO_3^-$ ), triiodide ( $I_3^-$ ), polyiodide ( $I_5^-$ ), (except molecular iodine ( $I_2$ )) are responsible for stain and unpleasant odour and has no degerming activity [8].

Molecular iodine ( $I_2$ ) in its non-charged form i.e.  $I_2$ , is preferred over other species of iodine because it is more permeable and possesses stronger chemical activity as an oxidizer, therefore it is more efficient in antiseptic and counter irritant activities. The negative charge of triiodide ( $I_3^-$ ) species, which is a key ingredient in many available iodine formulations, restricts its penetration through biological membranes, thus, it limits its efficacy as an antiseptic agent or counterirritant activity[9].

Molecular iodine ( $I_2$ ) kills all microorganisms by penetrating the cell wall and dislocates the cell's protein synthesis. It then proceeds to disrupt the cell's respiratory function and interfere with the lipid membrane and nucleic acid functions of microbes. Molecular iodine is preferred as antimicrobial, antiseptic and disinfectant and it rapidly constructive against all viruses, bacteria (both Gram positive and Gram negative), fungi and spores [10]. Molecular iodine ( $I_2$ ) is being tested and used against SARS CoV-2 and found to be beneficial in Covid-19 pandemic. It can kill all the viruses and can completely inactivate SARS CoV-2 with a 30 second exposure to 1-100 ppm molecular iodine ( $I_2$ ) [11] [4].

#### V. USES OF MOLECULAR IODINE ( $I_2$ )

**[1] AS SKIN ANTISEPTIC**-Molecular iodine ( $I_2$ ) is a broad-spectrum antimicrobial and acts as a skin disinfectant, protects the skin from microbial contamination. The stratum corneum of intact skin is an effective barrier against electrolytes; so molecular iodine is rapidly absorbed into the

epidermis when applied to the skin, stays in situ in solution, and maintains its biocidal activity and acts as a catalyst in the regeneration of lowerlayers of the skin by accelerating cell function [12].Once it is absorbed into skin it does not wash away with soap and water. Instead, it diffuses out of the skin slowly. The longer time taken by molecular iodine to completely diffuse from the skin ensures it exerts an antimicrobial effect that is sustained over long periods. On average a colloidal suspension of molecular iodine is active for 2 to 24 hours [12].

Being an antimicrobial, molecular iodine ( $I_2$ ) possesses counter-irritating activity in rheumatism, tenosynovitis and in inflammatory disease. It is used for disinfecting unbroken skin before operation, thermal burns, and herpes simplex, against skin lesions, UV irradiation, dendritic keratitis, cutaneous infections, and pre-operative treatment of thyrotoxicosis [13].

**[2] ORAL APPLICATION**-Molecular iodine ( $I_2$ ) is an asset antiseptic for treating periodontal diseases and many other oral infections. It extinguishes all periodontal pathogens in vitro within 15-20 seconds and it also exhibits an extensive viricidal spectrum involving both enveloped and non-enveloped viruses including periodontal pathogenic cytomegalovirus [4].

**[3] ACNE & DANDRUFF**-Acne involves the overgrowth and proliferation of skin microorganisms, primarily Propionibacterium Acnes. Molecular iodine ( $I_2$ ) with its antiseptic property eliminates Propionibacterium Acnes and also assists in modulating the hormones that cause acne and breakouts without the associated problems of long-term antibiotic use, and the development of antibiotic-resistance. Molecular iodine ( $I_2$ ) is cosmetically acceptable, affordable, and easy to use [14].

**[4] FOR AIR DISINFECTION**-Molecular iodine ( $I_2$ ) is found to be effective as an aerial disinfectant at concentrations much below its saturation vapor pressure. The maximum allowed concentration of iodine is  $1.0 \text{ mg/m}^3$ . East- Asia has developed and utilized molecular iodine-based procedures to disinfect air by iodine containing wall coatings,

ceramics loaded with molecular iodine, among other constituents [8].

**[5] MEDICAL EQUIPMENT STERILIZATION-**Molecular iodine ( $I_2$ ) has been preferred for disinfecting blood culture bottles and medical equipment, such as hydrotherapy tanks, thermometers, and endoscopes because of its non-staining properties [15].

**[6] FOR WATER DISINFECTION-**Molecular iodine ( $I_2$ ) is used to disinfect drinking water, swimming pool water as well as wastewater. Addition of molecular iodine tablets to the water followed by a 25-30 minutes disinfectant contact period before drinking is used. As molecular iodine does not react with ammonia or other nitrogen compounds, it is safe to use it as a swimming pool disinfectant. Recently, iodine resins are being used to solve the problems associated with water pollution caused by microbial residues. Molecular iodine in 1 ppm used for water disinfection is completely safe and it does not produce any colour, taste or odour and has no adverse effect on general health and thyroid function [8].

**[7] ENDOMETRITIS & MASTALGIA-**Molecular iodine ( $I_2$ ) has been used for vaginal disinfection for pre- & post examination during gynaecological procedures. Washing the vagina with a solution containing molecular iodine before a Caesarean delivery reduces the risk of endometritis (inflammation of the uterus). Research shows that taking molecular iodine reduces painful fibrous breast tissue. Taking 3000-6000 mg of molecular iodine for five months seems to scale back pain and tenderness in women with breast pain [16].

There are many other uses of molecular iodine which makes it ideal to be used as pharmaceutical and cosmeceutical acceptable molecule. Its advantage of non-staining and odorless behaviour helps in its broad coverage of therapeutic areas which makes it an interesting molecule in terms of drug discovery and screening.

## VI. SAFETY PROFILE OF MOLECULAR IODINE ( $I_2$ )

Molecular iodine ( $I_2$ ) is completely safe for use and non-toxic in nature. FDA has categorized molecular iodine ( $I_2$ ) under Category D. (NOTE: Category D= There is no evidence of human foetal risk but the potential benefits from use in pregnant women may be acceptable despite the potential risks (e.g., if the drug is needed in a life-threatening situation or for a serious disease for

which safer drugs cannot be used or are ineffective.)

Molecular iodine ( $I_2$ ) has a residual effect on topical administration which is caused by a dynamic back diffusion which is the reverse of the absorption occurring during application. Because of the stability issue of molecular iodine in aqueous media, molecular iodine is rapidly converted to iodide ( $I^-$ ) which results in severe pulmonary irritation leading to pulmonary oedema, but no such effect is seen by molecular iodine ( $I_2$ ) alone. Eye exposure to iodine species may result in severe ocular burns, but molecular iodine ( $I_2$ ) is found to be safe for use as an ocular antiseptic [13].

Molecular iodine precipitates cellular proteins of microbes and the affected cells may be killed, this effect is similar to that of a corrosive acid. Hence, it is used in antimicrobial contamination of tissues and cells. Molecular iodine ( $I_2$ ) can be absorbed by wounds and abrasions. Enhanced absorption occurs through denuded skin, decubitus ulcers, mucosal surfaces with high absorptive capacity (vagina), or large areas of intact skin. The transdermal absorption of molecular iodine ( $I_2$ ) is only 5% which is highly safe within the limits even on repeated use which can promote its usage as a broad-spectrum antimicrobial.

Whether iodine is administered topically or systemically, its other species like iodides can give rise to allergic reactions: urticaria, angioedema, cutaneous haemorrhage or purpura, fever, arthralgia, lymphadenopathy and eosinophilia, acne form or severe eruptions. But molecular iodine ( $I_2$ ) has no cytotoxic and anaphylaxis reaction reported or documented so far [13].

**CONCLUSION:** Molecular Iodine is free iodine present in nature which is a strong & broad-spectrum antimicrobial. Due to its good safety & tolerability profile it can be used topically in aqueous and non-aqueous solutions and has strong antiseptic & disinfecting properties, hence used against all viruses, bacteria and fungi. It is already proved to be active against Covid-19 and completely inactivated the virus with a 30 second exposure to 100 ppm molecular iodine ( $I_2$ ). It is also used in pre- and post-operative procedures to avoid microbial contamination and toxicity. Molecular iodine has no toxic effects and is extremely safe to use. The toxicity caused by iodine preparations is due to other species of iodine i.e., iodides & iodates. But all available iodine preparations contain a

blend of molecular iodine & the iodine species resulting in formulations which are effective as well as contain all the side effects. Its strong antimicrobial properties along with the absence of resistance to the pathogens make it a molecule of interest to be screened for multiple formulations in different approaches. In future formulations containing molecular iodine can be explored for its therapeutic & curative approach for short term & long-term therapies.

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