Resolving the paradox of iodine - an essential biomolecule

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Imprecise definition of Iodine is a major challenge to clinical application

The generalized use of the term "iodine" has prevented us from seeing molecular iodine's beneficial effects for too long.

The broad medical community considers the term iodine as any of many different topical antiseptics that stain the skin.

Among chemists, the use of this term is a long-standing abuse of iodine's nomenclature which generalizes every iodine species as "iodine".

This nomenclature generalization masks the complexity of iodine chemistry within the medical community and contributes to some avoidable adverse effects for patients.

Over 193 years ago, topical iodine compositions were invented. First Lugol's solution in 1829 and later tinctures of iodine [1]. Both brought formulations to the public that were clinically extremely useful but also associated with toxicity, irritation, and dark staining.

Molecular iodine (I2) was assumed to be the cause of the toxicity/ irritation and staining since it is the active biocide in both compositions [1]. When povidone-iodine (PVP-I) was created in 1955 it had lower concentrations of I2, and came with reduced staining, irritation, and toxicity [1]. It was viewed as a significant advance over previous formulations and the medical community correlated it as furtherproof of I2 "toxicity".

The lack of addressing specific iodine components makes it difficult to correct misconceptions and leads to miseducation surrounding iodine's properties of staining, toxicity, and biocidal activity.

Even in scientific manuscripts, the term iodine is used imprecisely, and can refer to several different chemical entities and complicated formulations that contain diverse iodine species. This imprecise description of iodine compositions may stem, in part, from ambiguous or deficient analytical characterizations. The USP method to measure I2 (thiosulfate titration) also detects triiodide (I) and hypoiodous acid (HOI). Consequently, clinicians do not know the concentration of active biocide (I2) in the iodophors they use. The equations that describe the equilibrium distribution of aqueous iodine species are non-linear and, as a result, only one predictive mathematical model exists [3].

Iodine exists in several oxidation states ranging from -1 (iodide) to +7 (e.g.: sodium periodate). With an oxidation state of 0, elemental iodine (I2), the active biocide in topical iodine compositions, is a blue-black crystal with a high metallic luster that sublimes readily to generate a violet-colored vapor.

In an aqueous environment, iodine exists in several different species. These include iodide (I-), molecular iodine (I2), hypoiodous acid (HOI), iodate (IO3-), triiodide (I3-) and polyiodides (I5- to I9-) [4]. They are characterized by different physical and chemical properties. The properties of an iodine containing composition can only be accurately assessed through analytical characterization for all ingredients [5, 6], the buffering capacity and osmotic strength.

In solution, the term "molecular iodine" or "free iodine" is used to refer to the I2 molecule. Its water solubility is limited due to its hydrophobicity and it reacts with water to form HOI. The reactivity of I2 in water is the single biggest challenge for topical iodine formulators. The chemical reactivity of I2 includes addition to double bonds, oxidization of sulphydral groups, addition to activated aromatic groups and formation of N-iodo derivatives.[7]

Behind the Research
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Research Focus

Dr. Kessler's expertise lies in the formulation of compositions that contain molecular iodine and in systems analysis of complex medical equipment.

He has successfully formulated pure I2 for a wide range of consumer and medical applications, taken a solid oral dosage form of I2 into phase III clinical trials and demonstrated that molecular iodine is not responsible for the staining and toxicity observed with topical iodine disinfectants.

His work includes the characterization of the structure-function of bacterial neuraminidase, the chemistry of iodination reactions in the follicular lumen and development of commercial products. He has utilized a variety of techniques to incorporate molecular iodine into different compositions and to characterize these materials.

Bio

Dr. Kessler has degrees in Chemistry from the Stevens Institute of Technology, Hoboken NJ (BS, 1972) and Biochemistry from S.U.N.Y at Syracuse, NY (PhD, 1980).

He has directed numerous teams focused on the formulation and development of animal and human drugs, managed joint venture programs for commercialized products and designed/managed Phase I, II and III clinical trials for a drug to alleviate breast pain.

His patents have been the basis of development of several iodine-based products including the Violet tablet, the ioRinse line of oral care products and the enzyme-based Iodozyme teat dip previously marketed by DeLaval. Dr. Kessler has also published basic and applied research on iodine formulations and the biochemistry of iodine/thyroid hormones.

He is currently the Chief Scientific Officer at I2Pure Corp. where he oversees and guides the development and commercialization of proprietary drugs and medical devices that deliver molecular iodine technology.

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