Resolving the paradox of iodine - an essential biomolecule

Blog Post 3 of 4 - Is "Tamed Iodine" a Red Herring?

The long-standing misuse of iodine's nomenclature within the scientific community has helped propagate untruths.

Among others, it obscures the full range of iodine species in povidone. Past formulations (e.g.: Lugol's solution and PVP-I) contain complexed elemental iodine and a diverse group of iodine species in equilibrium with molecular iodine.

When PVP-I was first formulated, it was deemed "tamed iodine", a reference to "taming" the staining, irritation, and toxicity. At the time, it was also assumed what needed to be "tamed" was molecular iodine. That has proven to be untrue [16]. Rather than neutralizing molecular iodine's "alleged toxicity", it's the triiodide molecules that are "tamed".

During formulation, triiodide molecules (which are toxic), attach to the polymer in PVP-I. This is the interaction responsible for any "taming" and the creation of a product less toxic, less irritating, and less able to stain than Lugol's solution or iodine tinctures.

Challenges to formulating molecular iodine

It is possible to formulate molecular iodine independent of the other iodine species found in topical iodine.

Upon study, molecular iodine is shown to (a) have mild toxicity, (b) not be the cause of the staining or irritation in povidone and (c) clearly demonstrates its biocidal activity [16].

I2 stability is the major technical challenge in designing topical iodine formulations. Hydration catalyzes I2 loss with the concomitant formation of HOI and ultimately hypoiodite, iodide and iodate [17]. This hydration reaction precludes commercialization of pure aqueous composition of I2 and is partially responsible for the subtle changes that occur in PVP-I compositions post-manufacture. Solid dosage forms designed to deliver I2 upon dissolution also have the potential to sublime or interact with moisture and reductants.

The four basic formulation strategies used to overcome I2 instability include using (1) iodide as a complexing agent [18], (2) organic complexing agents [19], (3) solid compositions that release elemental iodine slowly [20] and (4) oxidation reactions to produce iodine in situ [21-23].

Each approach has inherent constraints and potential benefits that need to be evaluated considering an intended application. Adopting a strategy that requires complexation of the I2 molecule with other species i.e., (a) and (b), makes delivery of pure I2 impossible. Iodophors like PVP-I are highly acidic compositions that provide relatively small concentrations of I2 in equilibrium with large concentrations of iodide/triiodide. The concentration of unbound I2 in 10% PVP-I is less than 8 ppm or less than 0.001% of the total iodine atoms present [24]. Iodophors manufactured with concentrations of I2 below a critical threshold (1 ppm) permit the survival of bacteria and transmission of nosocomial infections [25-28].

Regulatory agencies do not require vendors to provide a formulation of PVP-I [29] that would allow a practicing clinician to critically evaluate its suitability for sundry off-label clinical uses. Nuckolls [30] recently provided a description of the complex equilibria of the many iodine species that comprise a dilution of PVP-I and the risks associated with makeshift dilutions. A more rigorous analysis of the complex non-linear equilibria underlying aqueous iodine solutions has been provided by Gottardi [3] which demonstrates the sensitivity of the equilibrium to iodide and pH.

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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