Notes from the Oesper Collections

The Curious Case of Lloyd's Artificial Man

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The present generation hardly remembers the central role played by the American pharmacist, John Uri Lloyd (figure 1), in the scientific and cultural life of late 19th- and early 20th-century Cincinnati. Though he has been the subject of two book-length biographies (1, 2) and physical reminders of his legacy may still be seen in Cincinnati in the form of both the Lloyd Library on Plum Street and the Lloyd mansion in Clifton, few today can tell you who Lloyd was and why he was so influential in his day.

Born in New York State, but raised in rural Kentucky, Lloyd first came to Cincinnati in 1863 at age 14 to work as an apprentice for several manufacturing pharmacists. By 1886, he and his brothers, Nelson Ashley Lloyd and Curtis Gates Lloyd, were able to buy out the drug firm of Merrell and Thorp, which they renamed as Lloyd Brothers, Pharmacists, Inc. As Merrell had before him, Lloyd specialized in the manufacture of the plant extracts and tinctures favored by the Eclectic Medical Movement, which operated a medical school in downtown Cincinnati, where Lloyd also served as Professor of Chemistry.

Visibly active in the American Pharmaceutical Association and in various local scientific organizations, Lloyd became involved early in his career in an attempt on the part of the Eclectic movement to standardize its largely botanical pharmacopeia. His innovations in the preparation and standardization of plant extracts, such as his so-called "cold still" extraction process and his introduction of buffered alkaloids (Lloyd's reagent), soon established him as an expert in phytopharmacy – a reputation that was further reinforced by his founding of a major research library devoted to phyto- and botanical chemistry, a great outpouring self-published books and pamphlets - often stressing his own accomplishments - and his second career as a novelist. Though most of his novels, which were largely set in the rural Kentucky of his childhood, were only moderately successful, his 1895 "hollow-earth" fantasy – Etidorhpa – had some success, eventually passing through 18 editions and translation into seven languages.

To a modern-day chemist, the exact basis of Lloyd's scientific accomplishments remains something of a mystery.

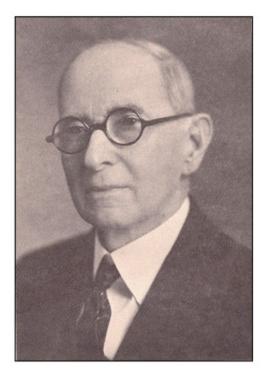


Figure 1. John Uri Lloyd (1849-1936).

As recounted in Margaret Kreig's popular book, Green *Medicine*, the investigation and assessment of a traditional plant or herbal remedy by the modern pharmaceutical industry requires proper clinical studies to determine its efficacy, followed by the extraction, purification, chemical characterization and synthesis and/or chemical modification of its active ingredient. Most of this is missing from the work of Lloyd – in part, because he lacked the formal chemical training necessary for such work and, in part, because many of the necessary techniques were unavailable for much of his early career. These limitations were endemic to the Eclectic movement as a whole, which, by the time of Lloyd's death in 1936, had largely collapsed as an legitimate alternative to mainstream medicine and pharmacy and whose remnants are now largely confined to the shelves of your local health food store.

Even in cases where Lloyd made interesting



Figure 2. Harry Shipley Fry (1878-1949).

discoveries or innovations, he often had to rely on the insights of others (for example Wolfgang Ostwald in the case of Lloyd's reagent) to provide the proper scientific rationale. And, of course, as a manufacturer of patent medicines, he also had to indulge in the usual advertising hype required to promote his products – a necessity often at odds with the exercise of proper scientific caution. The manner in which these limitations and conflicting demands could come into play is well illustrated by the curious case of Lloyd's so-called "Artificial Man" and its financial consequences for the head of the University of Cincinnati's Chemistry Department – Harry Shipley Fry (figure 2).

According to his first biographer, Corinne Simons, Lloyd had long been interested in the subject of iron-based "blood tonics" supposedly designed to reinvigorate "tired" or iron-deficient blood, as well as in the question of how sunshine might promote health and/or disease (1, 4). In 1919 Lloyd was joined in this quest by his son, John Thomas Lloyd (figure 3), who had been trained in limnology at Cornell University and who was teaching there when called home by his father to assist in the family business.

A more recent version of these blood tonics, which many readers may still remember, is the product known as *Geritol*, which gained national attention through its sponsorship of numerous television programs throughout the 1950s and 1960s, and notoriety when it was penalized with a \$812,000 fine by the Federal Trade

Commission in 1973 for advertising claims amounting to "gross negligence and bordering on recklessness." Indeed, the present author can recall being repeatedly dosed as a child with similar iron/plant extract combinations by his maternal grandmother – extracts which she routinely purchased from a mail order firm known as the Indiana Botanical Gardens.

Around 1926 the younger Lloyd prepared a series of blood tonics containing what he described as a "dispersion of catalytic iron" and which he claimed were stable "in the presence of acids, alkalis and tannin." Several corked bottles of this preparation where placed in the sunshine of a laboratory window for closer observation. After several hours the corks began to blow out of the bottles. Lloyd then prepared a second series of bottles, this time stoppered using a cork through which passed a short glass tube. Observation soon established that gas bubbles began to appear in these tubes about a half hour after the bottles were placed in the sunshine of the window, and that no gas was produced at night.

The Lloyds quickly jumped to the conclusion that they had discovered a key as to how iron in the blood interacted with sunshine and a potential solution to the questions which had occupied the senior Lloyd for so many years. As later described by Simons (4):

Thus it was that Lloyd's "artificial man" came into being. The bottle was filled with a fluid that repre-

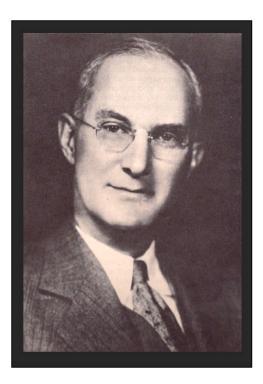


Figure 3. John Thomas Lloyd (1884-1970).

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sented the chemical affiliations of blood. Several of the "artificial men" were exposed to the sunshine. But nothing happened. No gas – no "breathing." Into one was put catalytic iron, the newly found "blood iron." In thirty minutes, bubbles flowed. When night came, the bubbles ceased. With the morning sun, they resumed ... This was their joint experiment which enabled scientists to determine the actual effect of light upon the human blood, the system and constitution, and to establish if sunshine may be responsible for disease in some cases and radiant health in others. In brief it discussed what one's daily dose of sunshine should be.

So convinced were the Lloyds of the scientific significance of their discovery that the younger Lloyd made the mistake of issuing a popular summary of their results to the syndicated press, which, in turn, rather predictably transformed it into a grotesque distortion of the actual events (4):

Using a bottle that "lives" in sunshine and "dies" in shade, two scientists have culminated nearly fifty years of research with the discovery of a mysterious gas, which may be exuded by all human beings, and which reacts in weird fashion to light rays.

Despite their initial enthusiasm and the resulting hype, the Lloyds soon had to admit that they both lacked the chemical expertise to properly unravel what was actually happening inside their so-called artificial man, finding instead that they had reached "the point where progress ceased and failure became static." As had been the case in the past, Lloyd now turned to others having more advanced chemical training, and offered Harry Shipley Fry, Head of the University of Cincinnati Chemistry Department, a small research grant to study what was really going on in their iron tonics. Fry used the grant to support a masters candidate in chemistry by the name of Elmer Gerwe, who summarized his findings in a M.A. thesis presented to the faculty in June of 1927 and in a paper jointly published with Fry in the December 1928 issue of Industrial and Engineering Chemistry under the title of "Action of Ultra-Violet Light Upon Ferric Citrate Solutions" (5).

No references to artificial men, mysterious gases, or the effects of sunshine on human blood are to be found in the paper by Fry and Gerwe. Instead the issue is presented as a problem of dealing with the photochemical stability of pharmaceutical preparations containing both ferric compounds and citric acid – both of which were apparently components of Lloyd's blood tonic. The authors were quick to point out that the photochemical reduction of ferric or iron(III) salts to ferrous or iron(II) salts in the presence of carboxylic acids,

such as oxalic, citric, tartaric and malic acid, had been known to photochemists since the 1870s.

In modern electronic terms, the Fe³⁺ ion and the citrate anion almost certainly form a complex of some sort in solution which is decomposed by the ultraviolet light in the sunshine, leading to reduction of Fe³⁺ to Fe²⁺:

$$2e^{-} + 2Fe^{3+}(sol) \rightarrow 2Fe^{2+}(sol)$$
 [1]

and the simultaneous oxidation of the hydrogen citrate ligand to acetone and carbon dioxide:

$$H(C_6H_5O_7)^{2-}(sol) \rightarrow (CH_3)_2CO(sol) + 3CO_2(g) + 2e^{-}$$
 [2]

with the latter product accounting for the observed bubbles formed whenever the artificial man was exposed to sunlight (6). Since this mechanism – though already proposed in the literature for the oxidation of citrate – was still somewhat speculative, the bulk of the paper was concerned with experimentally establishing that the molar ratio of Fe³⁺ used to the moles of carbon dioxide formed was indeed 2:3 as predicted by the proposed net equation.

It is of interest to note that this same photochemical reaction forms the basis of the photographic process known as "cyanotyping" or "blueprinting." First proposed by John Herschel in 1842, by 1915 the blueprint process was sufficiently widespread so as to be routinely described in high school chemistry textbooks and lab manuals (7).

Whatever his ultimate views concerning Lloyd's competence as a chemist, Fry had long been sensitized to his value to the chemistry department as a potential source of financial support and had been careful to cultivate Lloyd's good graces. Thus in 1924 an auto-



Figure 4. An autographed photo of Lloyd in his laboratory taken on the occasion of his 75th birthday in 1924 and presented to the students and faculty of the University of Cincinnati.

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graphed photo of Lloyd was requested to hang in the departmental conference room (figure 4) and he was also invited by Fry to serve as an honorary chairman for the 80th National Meeting of the American Chemical Society, which was held in Cincinnati in September of 1930 (8).

More serious, however, is the manner in which the incident of the artificial man revealed the rather naive folklore views held by Lloyd on such subjects as medicine, human physiology, and pharmacology – views which by the 1920s, at least, were woefully out of date. And it also calls to mind the fact that many years earlier Lloyd had used the vehicle of his novel *Etidorhpa* to express similar non-mainstream views on a variety of other scientific subjects, many of which could be uncharitably interpreted as bordering on pseudoscience (9).

References and Notes

- 1. C. M. Simons, *John Uri Lloyd: His Life and Works*, *1849-1936*, Privately Printed: Cincinnati, OH, 1972.
- 2. A. Flannery, *John Uri Lloyd*, *The Great Eclectic*, Southern Illinois University Press: Carbondale, IL, 1998.

- 3. M. Kreig, Green Medicine: The Search for Plants that Heal, Rand McNally: Chicago, IL, 1964.
- 4. Reference 1, pp. 116-118. Regrettably Simons is often hopelessly vague in her descriptions and also fails to reference her sources, so some caution is necessary when citing her version of events. Unfortunately the present-day Lloyd library reports that it has no files or press clippings relating to the story of Lloyd's "artificial man."
- 5. H. S. Fry, E. C. Gerwe, "Action of Ultra-Violet Light upon Ferric Citrate Solutions," *Ind. Eng. Chem.*, **1928**, 20, 1392-1394.
- 6. In the actual paper, Fry used traditional molecular equations rather than net ionic half-reactions. Hence the Fe³⁺ concentration was instead formalized in terms of the salt $Fe_2(SO_4)_3$ and the reaction stoichiometry in terms of a predicted 1:3 molar ratio of this salt to the moles of CO_2 formed.
- 7. See, for example, R. B. Brownlee, R. W. Fuller, W. J. Hancock, M. D. Sohon, J. E. Whitsit, *First Principles of Chemistry*, Allyn & Bacon: Boston, 1915, pp. 380-381.
- 8. W. B. Jensen. "The 1930 Cincinnati Meeting of the ACS," *The Chemical Bond*, **1988-1989**, *23*, 11-14.
- 9. J. U. Lloyd, *Etidorhpa or the End of Earth*, 3rd ed., Caxton Press, 1902. See especially Chapters 44-54.