ON THE (IGNORED?) ROLE OF CARBON SURFACE CHEMISTRY IN BIOMEDICAL ADSORPTION APPLICATIONS: A REVIEW IN TRIBUTE TO F. J. DERBYSHIRE

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Introduction

Among the most treasured legacies of the late Frank Derbyshire, the scientist-turned-administrator, is one that stems from his cosmopolitan character and his broad range of scientific and cultural interests: his emphasis on the interconnected and holistic nature of scientific research. The most conspicuous example is the connection between coal research and carbon research, which was largely responsible for the successes of his Center for Applied Energy Research in the last decade. The resulting synergisms are certainly worth analyzing in some detail, but the topic of my presentation is a less obvious example, perhaps an even more dramatic one, and certainly one that is more appropriate for this conference and its format, having as its kickoff event a special symposium on carbon in biomaterials. From the conversations with Frank in the early stages of preparation for Carbon 2001, I remember well his enthusiastic plans for bringing together the biomedical and carbon research communities. His instincts told him that one of the next big frontiers in carbon research is right there, at that interface. And was he right, indeed! Here are some of the reasons, already anticipated by Derbyshire et al. [1] in a brief section entitled "Medical Applications of Carbon" of this posthumously published review.

Biomedical Adsorption Applications

Even though "carbon, especially activated carbon in the form of charcoal, has been used in medical and health applications for centuries" [1], the first landmark papers on this topic are from the mid-1940's [2,3]. It turns out, however, that these papers were completely ignored by the carbon research community. The next landmark publication was Cooney's monograph [4], which again has been largely ignored by carbon researchers (*hélas*, including myself [5]). While Derbyshire et al. [1] cite a handful of publications from the 1980's dealing with applications of activated carbons in deodorization, haematology, haemodialysis and drug delivery systems, it is really in the last decade that a flurry of research activity in both communities has finally allowed us to see the synergism and start building bridges which will lead to optimized and exciting new products. In particular, recent advances in our understanding of carbon surface chemistry [6] and liquid-phase adsorption phenomena [5], which in turn have heretofore been largely ignored by the biomedical research community, should make these developments much easier. Several concrete examples will be offered during the presentation.

Treatment of Intoxication

Figure 1 reproduces the *in vitro* results from Andersen's pioneering study of adsorption of alkaloid salts, barbituric acid derivatives, metal salts and other substances on two different carbons. The author concluded that "the various charcoal preparations appear to vary considerably in their capacity for adsorption." Half a century later (and with only 30 citing papers registered by the Science Citation Index in the period 1964-2000, none of them in non-medical journals), are we in a position to reach a more profound conclusion? Here is a relevant quote from a recent Position Statement endorsed by the American Board of Applied Toxicology [7]: "The adsorptive surface of activated charcoal contains several carbon moieties (e.g., carbonyl, hydroxyl) that adsorb a poison with varying affinity... In vitro adsorption to activated charcoal in aqueous solution is a non-specific process that reaches equilibrium in less than 30 minutes." The internal (and external!?) consistency of these two statements is certainly deserving of greater scrutiny. Another recent paper [8], with an ambitious title ("Selection of activated charcoal products for the treatment of poisonings"), contains the following (anticlimactic?) conclusions: "Not all activated charcoal products are alike... Although increasing the surface area ... should increase its effectiveness, no differences among the current formulations are apparent in published studies... Additional studies are needed to identify the relative advantages of currently available activated charcoal products." In contrast, Cooney [9] reported that the "product containing a 2000 m^2/g charcoal ... adsorbed more drug per unit volume of suspension than did the ... products [that] contained 900 m^2/g charcoal and which were all similar in performance."

Haemodialysis

The literature on carbon use in haemodialysis (and/or haemoperfusion) is more recent. It also may be poised for exponential growth, having in mind the very recent federal advisory panel recommendation [10] that FDA mandate the filtering of donated blood (leukoreduction) to minimize risks associated with transfusion. The pioneering study is that of Yatzidis [11], with 209 citing references, only 34 of which are from the period 1986-2001, and none of which are in non-medical journals. In 1991 the assessment of Ash et al. [12] was that "[c]harcoal hemoperfusion, hemodialysis, hemofiltration, and plasmapheresis have been tried, but benefits have been short-lived and outweighed by deleterious effects." These authors studied neurologic improvements of patients with hepatic failure and did find that the combined use of "cellulosic membranes with a suspension of powdered charcoal and cation exchanger... can be used as a bridge to allow time for intrinsic liver recovery, or to permit an optimally successful liver transplant procedure."

Drug Delivery Systems

This is the most recent and in many ways the most demanding application. In addition to the more conventional direct injection of anticancer drugs [13], there is much interest in magnetic drug targeting. Early magnetically targeted carriers (MTC), albumin microspheres (0.2-2 μm), contained both Fe_3O_4 particles (10-20 nm) and a chemotherapeutic agent entrapped in the albumin matrix [14,15]. Figure 2 compares their doxorubicin (adriamycin) adsorption capacity to that of carbon-based adsorbents [16,17]. The rationalization of these differences and the opportunities for optimized adsorption and desorption are very much virgin research territory, however.

Figure 1. Uptakes of toxic substances (in mg/g) by carbon A ("Carbo med. Merck") and carbon B ("charcoal preparation X"). From Ref. 2.

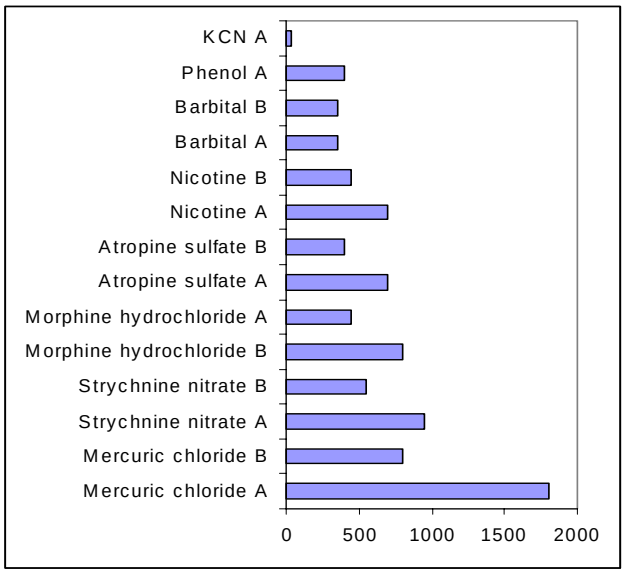

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Figure 2. Doxorubicin uptake (in mg/g) by several drug carriers. From Refs. 14, 16 and 17. (Surface areas provided in parentheses.)