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Current Commentary

Rates of pharmacokinetic literature obsolescence

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Summary

Obsolescence may be defined as the decline over time in validity or utility of information. To investigate pharmacokinetic literature obsolescence, two discrete methodologies were utilized. In the first type, the age distribution of 12,836 periodical references from 766 pharmacokinetic papers published in 16 journals and bearing a 1982 publication date was analyzed (synchronous study). The median reference citation age was 4.52 years, and 54.4% of all citations were to articles published in the prior 5 years. Using non-linear regression analysis, two groups or types of literature were tentatively identified. The first or 'ephemeral' type comprised about 98.5% of the sample and obsolesced with a 2.94 year half-life. The second or 'classic' type comprised about 1.5% of the literature and obsolesced with a 21.6 year half-life (there was, however, considerable imprecision in this latter parameter estimate). A historical or diachronous study followed quantitative citation patterns to 6 classic pharmacokinetic articles published in the 1960s. Citation counts were normalized to eliminate the influence of pharmacokinetic literature growth. The harmonic mean obsolescence half-life was 2.24 years. The results of both the synchronous and diachronous studies strongly suggest pharmacokinetics is characterized by an unusually high degree of rigor in methodology and data analysis, i.e. pharmacokinetics is a relatively 'hard' discipline.

Introduction

The growth of pharmacokinetic literature over the past 10–15 years has been substantial. For example, the estimated 1270 papers published in 1980 represented a

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2.5-fold increase over the 1975 rate (Boxenbaum, 1982). Obviously, a rapid growth of new literature accelerates the obsolescence of existing work. In this regard, there are at least two types of obsolescence (Storer, 1967). The first occurs when concepts and interpretations of data from particular articles are updated and/or carried forward by other investigators. The second type occurs when the subfield of knowledge is either misguided or incorrect. In either case, the tendency is for older papers to be cited less frequently than contemporary work. Obsolescence may thus be defined as the decline over time in validity or utility of information (Line and Sandison, 1974).

The rate of literature obsolescence in a scientific discipline seems to be related to its 'hardness' or 'softness' (O'Connor and Voos, 1981; Price, 1970; Storer, 1967). Hard sciences are characterized by a high degree of rigor in methodology and data analysis and generally involve a great deal of mathematics. Soft sciences generally deal with more complicated and diffuse subject matters not readily reduced to mathematical formulae. Disciplines relying on and citing recent references in their papers are considered to be at the research front as hard science. Disciplines with references to more retrospective materials are considered soft and less scientific. Soft sciences include psychology, sociology and political science. Examples of medium hard sciences are botany, zoology and economics. Traditionally hard sciences include physics, chemistry and biochemistry.

Within many scientific disciplines, two distinct types of literature may be distinguished, classic and ephemeral (Burton and Kebler, 1960: Price, 1965). Classic literature has more impact and staying power, whereas ephemeral literature is readily replaced with newer work. The literature of mathematics, geology and botany contains considerably more classic literature than does chemical, mechanical and metallurgical engineering and physics; chemistry and physiology fall between these 2 groups.

Literature obsolescence may be investigated from 2 perspectives, synchronous and diachronous (Gapen and Milner, 1981; Line and Sandison, 1974). Synchronous studies analyze the age characteristics of references cited over a fixed period in time, say, over a given 1 year period. Diachronous studies follow the utility of particular books or articles over their useful life span. Therefore, synchronous studies investigate generalized reference patterns retrospectively, whereas diachronous studies look at citation patterns of distinct reference materials at dates future to their publication. The results of synchronous and diachronous studies need not be the same and frequently show marked differences.

This report investigates pharmacokinetic literature citation patterns from both a synchronous and diachronous perspective. Using literature obsolescence criteria, it will be demonstrated that pharmacokinetics is a very hard science, and that the ratio of ephemeral to classic literature is approximately 67 : 1.

Methods

A previous study (Boxenbaum and Pivinski, in press) collated all dated reference materials (14,546 citations) to 766 pharmacokinetic papers published in 16 journals

bearing a 1982 publication date. Citations to undated work that was either not published, submitted for publication, accepted for publication or in press were not included in the sample. It was estimated that these 766 papers represented 56% of the total 1982 pharmacokinetic periodical literature. Of these citations, 88% or 12,836 were to periodicals. The age distribution of these periodical citations (synchronous study) were determined manually. Visual inspection of a semilogarithmic plot of frequency of citation (citation count) vs age of publication suggested a triexponential function would characterize the curve, and this was reinforced by computer analysis with CSTRIP (Sedman and Wagner, 1975). The year 1985 was arbitrarily set to zero, and the age was taken as the difference between 1985 and the year of citation. Consequently, a lag time was required. Using the lag time, coefficients and exponents from CSTRIP as initial estimates, a triexponential function was fitted to the data using NONLIN (Metzler et al., 1974). Unlike conventional pharmacokinetic curves resulting from extravascular drug administration, the sum of the coefficients was not required to equal zero. The dependent variable was weighted by its reciprocal and by its reciprocal squared. The fits were virtually the same, and only the results of the former weighting scheme are reported.

A diachronous study of 6 classic papers published in the 1960s was also undertaken. Yearly citation counts were made from Science Citation Index. Since the pharmacokinetic literature grew substantially after the 1960s (Boxenbaum, 1982), so did citations to these papers. To correct for the influence of pharmacokinetic literature growth, yearly citation rates were divided by the estimated number of pharmacokinetic papers published each year. The latter values were estimated from a logistic relationship (Boxenbaum, 1982):

$$N = N_{max}/[1 + e^{-(\alpha+\beta t)}] \quad (1)$$

where N is the estimated number of pharmacokinetic papers published in year t, N_{max} is the logistic curve's asymptote of 1450, and α and β are parameter estimates of -6.73 and 0.510 years^{-1}, respectively. For mathematical purposes, zero time was taken as 1963, so that t was equal to the year of publicaton minus 1963. Dividing citation counts by estimates of N has the effect of removing the growth feature from this analysis of obsolescence. This is in contrast to the synchronous study, were literature growth is an important variable and contributes significantly to the results.

Monoexponential decay patterns for normalized citation rates were observed with all 6 papers of the diachronous study, and parameters were estimated using unweighted linear regression analysis of logarithmically transformed data.

Results and Discussion

The data and results of the synchronous study are illustrated in Fig. 1. Peak citation rate occurred on the theoretical curve at 2.85 years. This is in agreement with most studies (Braun and Bujdosó, 1982; Brown, 1980; Margolis, 1967; Garfield, 1979) that indicate articles usually show a maximum rate of citation at 2–3 years

after publication. The second and third exponential terms of the equation indicated in Fig. 1 are measures of the decay of literature citations with age (obsolescence). The two half-lives of the exponential terms are 2.94 and 21.6 years, and the coefficients have a ratio of 67 : 1, respectively. It is hypothesized that the 2.94 year half-life reflects obsolescence of the 'ephemeral' literature, and the 21.6 year half-life reflects the obscolescence of the 'classic' literature. The percent coefficient of variation for the rate constant reflecting decay of the hypothesized classic literature is 189%, indicating considerable imprecision of this estimate. The coefficient ratio of 67 : 1 indicates that only about 1.5% of the literature cited by pharmacokineticists is classic. From results of a previous study (Boxenbaum and Pivinski, in press), it appears that this latter category would include a review article on physiological approaches to hepatic clearance (Wilkinson and Shand, 1975) (the most cited paper in pharmacokinetics in 1982). Articles not predominantly pharmacokinetic in nature but nonetheless useful to pharmacokineticists, can also be classics. These include a paper on the measurement of protein concentrations (Lowry et al., 1951), a review article on microsomal enzyme induction (Conney, 1967), and a method for analyzing protein binding data (Scatchard, 1949).

Since the preponderance of citations in pharmacokinetic literature is to work predominantly pharmacokinetic in nature, and because about 98.5% of the literature decays into obsolescence with a 2.94 year half-life, pharmacokinetics may be regarded as an extremely 'hard' science. This position is reinforced by contrast to a 3.8 year half-life for references within radioanalytical articles (hard science) published in 'Analytical Chemistry' during 1972–1974 (Braun et al., 1977). Other citation indices of hardness are also in accord with this view. The median citation

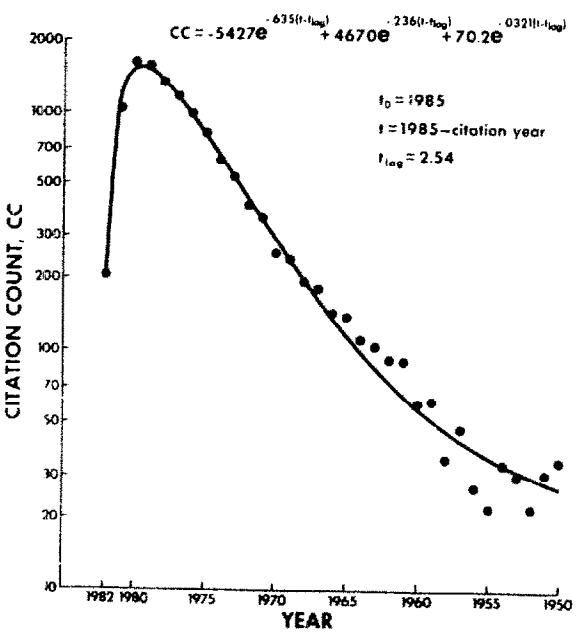

Fig. 1. Synchronous pattern of pharmacokinetic literature growth and obsolescence for the year 1982. See text for discussion.

TABLE 1

DIACHRONOUS CITATION HALF-LIVES (ADJUSTED FOR LITERATURE GROWTH) FOR THE DECAY OF CLASSIC PHARMACOKINETIC ARTICLES

Values for P were less than 0.001 in all regressions, and correlation coefficients were all above an absolute value of -0.950. See text for discussion.

Article	Half-life (years)
Loo, J.C.K. and Riegelman, S., New method for calculating the intrinsic absorption rate of drugs. J. Pharm. Sci., 57 (1968) 918–928.	3.51
Nelson, E., Kinetics of drug absorption, distribution, metabolism and excretion. J. Pharm. Sci., 50 (1961) 181–192.	1.56
Riegelman, S., Loo, J.C.K. and Rowland, M., Shortcomings in pharmacokinetic analysis by conceiving the body to exhibit properties [illegible] compartment. J. Pharm. Sci., 57 (1968) 117–123.	2.91
Wagner, J.G., Biopharmaceutics: absorption aspects. J. Pharm. Sci., 50 (1961) 359–387.	1.61
Wagner, J.G. and Nelson, E., Percent absorbed time plots derived from blood level and/or urinary excretion data. J. Pharm. Sci., 52 (1963) 601–611.	2.21
Wagner, J.G., Northam, J.I., Alway, C.D. and Carpenter, O.S., Blood levels of drug at the equilibrium state after multiple dosing. Nature (Lond.), 207 (1965) 1301–1302.	2.98

age in this survey was 4.52 years, and 54.4% of all citations were to articles published in the prior 5 year period (Price index). Moreover, pharmacokinetics makes extensive use of mathematics, and this is a characteristic of hard science.

One may postulate that during the early developmental stage of pharmacokinetics, say 1964–1968, that the rate of synchronous decay was slow; this would have resulted from there being a rather small pool of relevant literature. Consequently, authors would have cited literature from other sources, including a significant proportion from older sources. As pharmacokinetics matured and the literature expanded, authors could concentrate their references on more recent and relevant work (Gama de Queiroz and Lancaster, 1981).

Table 1 summarizes half-lives for the diachronous citation decay of 6 classic articles appearing in the pharmacokinetic literature during the 1960s. The harmonic mean half-life for the sample is 2.24 years. Unlike the synchronous study, the diachronous data could be adjusted for growth in the pharmacokinetic literature. These half-lives therefore reflect obsolescence in the absence of literature growth. The diachronous study results do *not* imply obsolescence of the informational content per se, but rather reflect a tendency by pharmacokineticists to cite updated or summarized information in other articles and textbooks or to omit citing references once the information is perceived to be integrated into the general body of knowledge—this latter phenomenon is termed 'obliteration' (Garfield, 1979). The short harmonic mean half-life of 2.24 years is consistent with a rapid turnover time (3.23 years) of information in a hard scientific discipline like pharmacokinetics.

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