

## **Bias in traditional medicine in East Asia**

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*The statement that traditional East Asian medicine has a history of several thousand years can operate as a bias. However, there is also a «publication bias» stemming from the imbalance between formally tested traditional drugs and informally accumulated historical knowledge. Randomized controlled trials on traditional Kampo drugs must be done. In the meantime, the truth about the efficacy of both modern and traditional drugs does not lie in a single formal study, but lies in the continuous circle of experience and re-evaluation - from phase I data to phase IV data.*

Being the only *Japanese* contributor to this book, I would like to describe briefly how PARACELsus is known in Japan. I did a computer search using the keyword «*Paracelsus*» in the data base called JBCAT - Japanese Book CATalogue, a service provided by the *National Centre for Sciences Information Systems* called «*NACsis*». The print-out showed nine books on PARACELsus published in Japan. The first one was published in 1943 and was a translation of the book by STILLMAN. So far, seven translations and two original books written by Japanese authors have been published in Japan, with revised editions.

In my University library I could find among others a Japanese translation of the book by ERNST KAISER, and a book written by H. OHASHI, a Japanese psychiatrist. The latter book is an original Japanese one.

I could extract another kind of print-out from the mentioned database, listing the libraries where the books are held. For example, the Japanese translation of JUNG's «*Paracelsica*» can be found in more than 40 Japanese university libraries. Japan has an advanced information retrieval system. The Japanese counter-part of MEDLINE is called JMEDICINE, often abbreviated as JMED. It is a potential source for clinical epidemiological research on traditional medicine in East Asia and of its (rational) use. Some of these databases are now accessible through international networks like «*Internet*». However, most of the databases are in Japanese.

Now, I will discuss two kinds of biases concerning traditional medicine in East Asia, and I particularly refer to *China* and *Japan*. These biases, up to now, have prevented a rational use of and research on East Asian medicine.

The *first bias* is the statement that traditional East Asian medicine has a history of several thousand years. This is commonly said by researchers, citizens, and even politicians in East Asia, and sometimes by Western researchers.

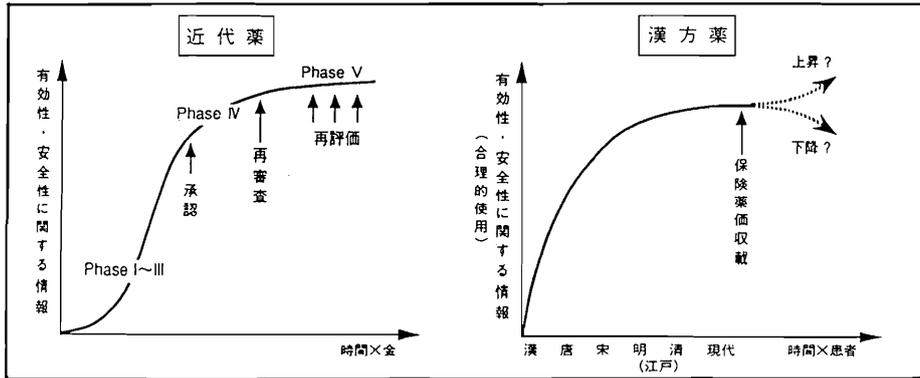


Fig. 1: Growth of information in modern (left) and traditional (right) drugs

The diagram in Fig. 1 shows on the left the growth of information on the safety and efficacy of a modern drug. The vertical axis represents the quantity of information from phase I studies to phase II and phase III, and when it reaches an acceptable level, it is approved for marketing by the drug regulatory authority. It also includes information on phase IV studies, i.e. post-marketing surveillance. The horizontal axis represents the resulting product of time multiplied by money.

In contrast, the diagram shows the information growth regarding traditional drugs on the right. Here, the horizontal axis is a product of time (length of use) multiplied by the number of patients using traditional drugs. The horizontal axis goes from the *Han dynasty* to *Tang, Sum, Ming, etc.* to the modern time. Information has been accumulated since the *Han dynasty* in China two thousand years ago, and this system was introduced to Japan one thousand years ago. And since 1976, *Kampo* drugs, the Japanese variation of Chinese drugs, have been covered by the National Health Insurance Scheme. The decision to include *Kampo* drugs in the National Health Insurance scheme was based on historical experience, not on (randomized) controlled trials. After that, the consumption of *Kampo* drugs nearly doubled every year, and now, more than one billion US dollars are spent annually on these drugs, or roughly ten US dollars per person. This growth is partly due to the aggressive sales promotion and also due to the complicated health insurance scheme which spends more money if physicians prescribe more drugs.

I have strong doubts whether the rationality in the use of traditional drugs has improved since 1976. The vertical axis of safety and efficacy is closely related to the rational use of drugs, including the five aspects quality, safety, efficacy, cost, and information.

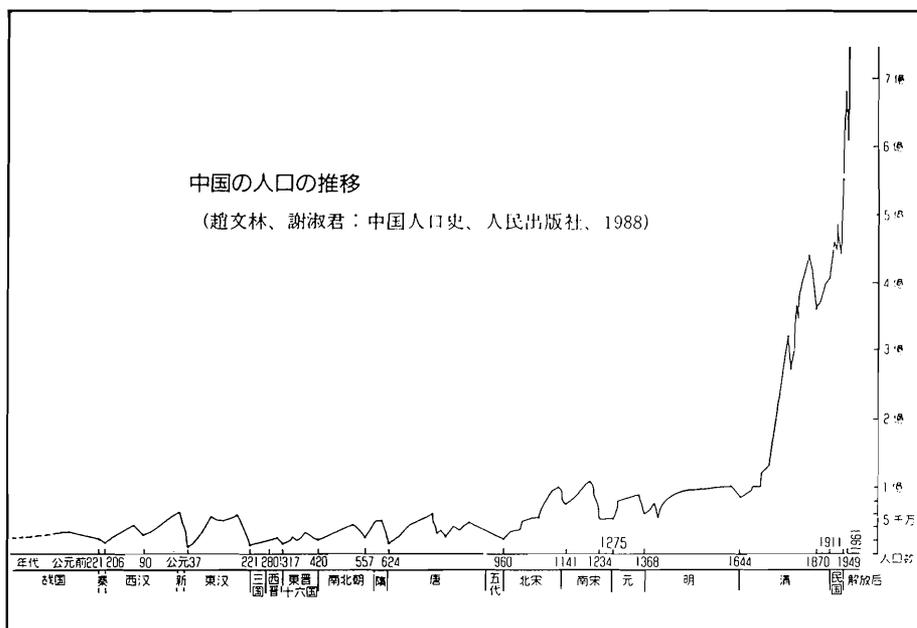


Fig. 2: Population growth in ancient and modern China

Figure 2 shows the population development in China since the time before Christ. The data come from tax documents from ancient China. In 140 B.C. the famous «Shanhanlun», the classic of Chinese medicine writing. Information on the safety and efficacy of traditional drugs has basically been produced by the experience of their use by humans.

This chart reminds us that the amount of experience gained can be numerically analysed. You may already have realized that the safety and efficacy of drugs is based, not on the length of their use, but on the product of the time multiplied by the number of patients who actually used them. We may use pharmaco-epidemiological methods to analyse this information growth. If we can find information about disease patterns and the quantity of drugs used in a particular time and region of ancient China, we may find out more about the efficacy and safety of traditional drugs. I think the amount of bias in ancient times is much less than that of today. Here, today we have a very strong bias produced by

industry, by ambitious researches, or by the so-called «new age» movement which favours traditional herbal medicine.

PAUL COHEN of the *Wesley University* in the United States wrote in his book «Discovering the History of China» (1984) that Americans' view of China has changed, reflecting their own socio-political attitude. The Japanese translation of his book has a slightly modified title: «Intellectual Imperialism», sub-title: «Orientalism and Image of China». I think the Westerners' view, particularly in the US, has changed since the Vietnam war. And myself, I believe that their view on traditional medicine in Asia is now sometimes too generous, too sympathetic and emotional. This reflects a loss of trust in their own sciences which to some extent has created an inhuman and cold atmosphere and adverse reactions in the medical field. I think the value of a drug lies in its usefulness, no matter how old or how new it is. That is why I recommend to the physicians in Japan, as well as to the pharmaceutical industry and the government, that they should conduct randomized controlled trials of *Kampo* drugs.

The *second bias* we have to consider is the *publication bias* in the results of modern drugs, and extended to traditional drugs, the bias from the imbalance between formally tested drugs and indications and informally accumulated historical knowledge. Thus, putting too much weight on published studies by ignoring unpublished studies or less formally accumulated historical knowledge and experience leads to a biased comparison of Western drugs with traditional drugs.

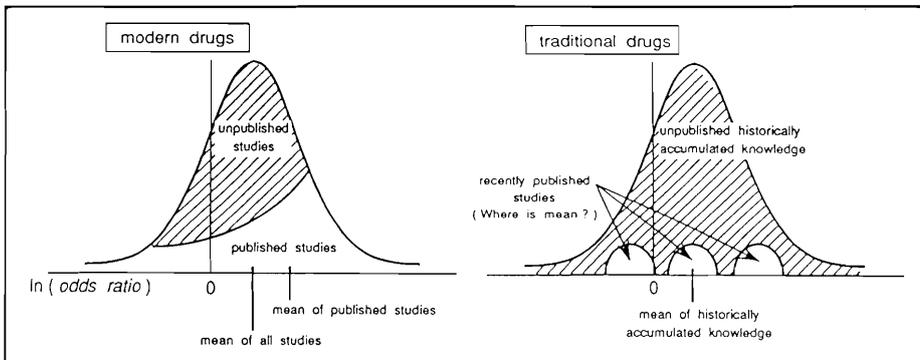


Fig. 3: How publication bias affects modern drugs compared to traditional drugs

The diagram on the left in *Fig. 3* shows the concept of publication bias of modern drugs. It is widely known that negative study results are less likely to be published. Thus the mean effectiveness of published studies is usually higher

than the mean of all studies. This does not necessarily represent the truth of the parent population. This is a serious problem particularly in meta-analysis.

The diagram on the right shows the current state of randomized controlled trials of traditional drugs in East Asia. So far in Japan, only about sixty controlled studies of *Kampo* drugs have been conducted, including studies in which the randomization method was not well described. Out of the sixty, only about ten are of high quality with proper randomization and blinding, proper monitoring and statistical analysis and interpretation. As the number of such studies is so small in comparison to the information which is historically accumulated, we cannot establish the validity. It may still be too early to make a final judgement on the value of traditional drugs in East Asia. Although meta-analysis is a powerful and sophisticated method, we still have to interpret the results carefully.

How can we bridge the gap between historical accumulated knowledge and the scarcity of randomized trials? I practice some *Kampo* medicine myself, without having solid data based on randomized controlled trials. So, should I stop practicing *Kampo* medicine because there are so few randomized trials, or should I continue to practice it as it has a long history? How can I feel comfortable in this situation?

Figure 4 shows the information cycle on new drug developments from the ecological point of view. Based on the non-clinical studies, phase I studies are conducted, followed by phase II and phase III studies. Bias and delay may occur at any time during these phases until the drug finally reaches the consumer. But this is not the end. Information is still collected and other studies are conducted in phase IV post-marketing surveillance, and information is fed back to the earlier phases. For instance, if there is a finding indicating new effects and indications of a drug, such information is considered exploratory data, and one has to go back to earlier phases to confirm its efficacy. It is important to note that there are no *rational drugs* as such, but only a *rational use* of drugs.

Basically, I think these information cycles should be the same in modern and traditional medicine. If we have a good ecological system, say a forest (see fig. 4), the system can produce not only timber, but fish, prawns, shellfish and others. I think the truth of both modern and traditional drugs does not lie in the single study, but lies in this type of cycle. Thus, my practice of *Kampo* medicine also evolves around this cycle. This cycle in traditional drug evaluation should be made more efficient to increase the reliability of the information.

After having reached this conclusion I feel comfortable with my daily practice of *Kampo* medicine in Japan.

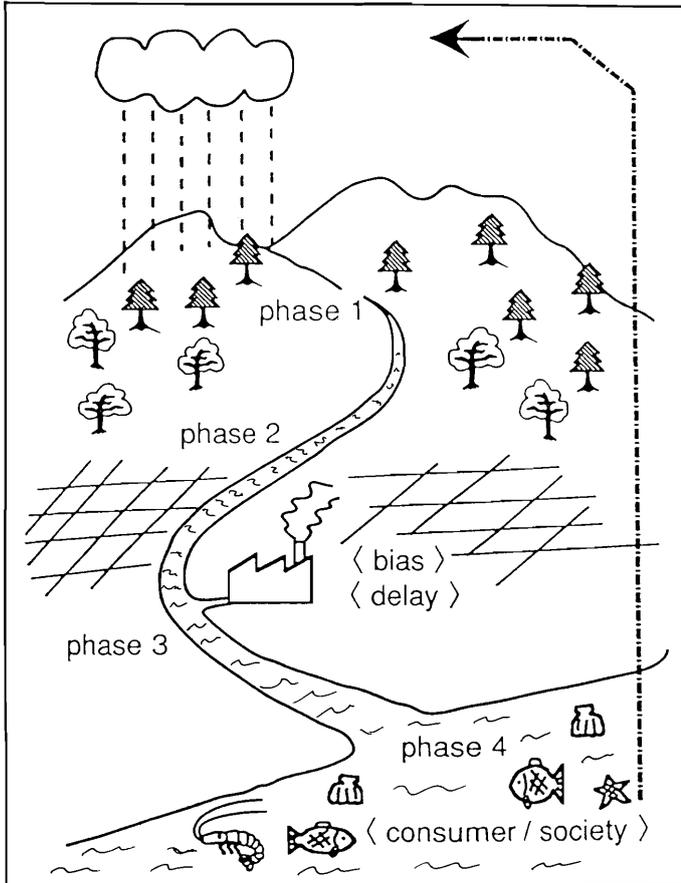


Fig. 4: The ecology of drug information accumulation

Further reading

TSUTANI K. The evaluation of herbal medicines: An East Asian perspective. In: Lewith GT, Aldridge D (eds). *Clinical research methodology for complementary therapies*. Hodder and Staughton, London - Sydney - Auckland 1993: 365 - 393