

This Week's Citation Classic

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Flower R J. Drugs which inhibit prostaglandin biosynthesis.

Pharmacol. Rev. 26:33-67, 1974.

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This was the first review to draw together all the data then available on the inhibition of prostaglandin biosynthesis by aspirin-like drugs and other compounds. It aimed to provide a useful guide to biological scientists who wished to use these drugs as pharmacological tools. Much of the subject matter has been reviewed several times since then. Reference 1 is a particularly comprehensive article. [The *SCI*[®] indicates that this paper has been cited in over 905 publications since 1974.]

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"When I was told that this paper had become a *Citation Classic*, I was both surprised and a little amused, for the review started out as a sort of private student project.

"I began my PhD studies with John Vane at the Royal College of Surgeons in 1971. He and his colleagues had just made their fundamental discovery that the aspirin-like drugs prevented prostaglandin generation by blocking the biosynthetic cyclo-oxygenase enzyme.^{2,4} His department of pharmacology was a very busy and exciting place to work in those days, and the notion that inhibition of prostaglandin generation could explain the anti-inflammatory effects of aspirin was one of the hottest concepts of the time.

"I began my postgraduate work by examining the effects of many anti-inflammatory drugs on the prostaglandin synthesizing system and was fortunate to be able to contribute to several significant publications on the topic (e.g., reference 5). In my spare time, I began to collect together all our results and those published by other groups and arrange them into tables; I also collated a lot of data about inhibition of the enzyme by other agents such as fatty acid analogues and antioxidants.

"Apart from my enthusiasm for the subject, my motive for doing this was laziness. I thought that if I could sort out all this data a little at a time, it

would save me a great deal of effort later when I came to write my PhD thesis! Eventually, however, the idea that my Sunday afternoon jottings might be put together into some sort of review began to claim my attention. With the help of a senior colleague, Mick Bakhle, I prepared a manuscript and later showed it to Vane. After he had read it and suggested various changes, he surprised me by suggesting that it might be suitable for *Pharmacological Reviews*. I was even more surprised when it was accepted almost immediately by that august journal.

"The literature on prostaglandins absolutely exploded in the early 1970s. Because prostaglandins are formed by practically every tissue in the body, one cannot resort to the techniques of classical endocrinology (i.e., removal or ablation of a particular gland or organ) to test for their involvement in physiological events. Neither were there any really reliable antagonists of prostaglandin action, and so the key to many experiments was the use of the aspirin-like drugs to prevent the cellular biosynthesis of these lipids. Naturally, many scientists wanted to know what dose of these drugs to use, how long they would last, or what the likely side effects were. Because of this demand for information my little review was warmly received and, it now appears, highly cited. Incidentally, I am not sure whether it is always strictly ethical to cite reviews: I often notice that people refer to this particular manuscript as if it were the source of the original information, instead of citing the author who first published the data. This use of comprehensive reviews as 'umbrella references' undoubtedly gives them a spurious citation score.

"The entire prostaglandin system has become much more complex than it was in 1974. Thromboxane and prostacyclin have been discovered and a plethora of new lipooxygenase enzymes have also made their appearance, adding substantially to the number of target enzymes in the cascade.

"Sometimes I think it would be a good idea to update the review to include inhibitors of all these new pathways. Rash impulses like this are easily checked: I stand by an open window in our library, take several deep breaths, and thumb through the latest *Current Contents*[®]. The sight of all those new papers on prostaglandins is enough to strike terror into the heart of the most seasoned reviewer!"

1. Shen T Y. Anti-inflammatory drugs. (Vane J R & Ferreira S H, eds.) *Handbook of experimental pharmacology*. Vol. 50 (II). Berlin: Springer-Verlag, 1979. p. 305-42.
2. Vane J R. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. *Nature New Biol.* 231:232-5, 1971.
[Citation Classic. *Current Contents/Life Sciences* 23(42):12, 20 October 1980.]
3. Ferreira S H, Moncada S & Vane J R. Indomethacin and aspirin abolish prostaglandin release from the spleen. *Nature New Biol.* 231:237-9, 1971.
4. Smith J B & Willis A L. Aspirin selectively inhibits prostaglandin production in human platelets. *Nature New Biol.* 231:235-7, 1971.
5. Flower R, Gryglewski R, Herbaczynska-Cedro K & Vane J R. Effects of anti-inflammatory drugs on prostaglandin biosynthesis. *Nature New Biol.* 238:104-6, 1972.
[The *SCI* indicates that this paper has been cited in over 330 publications since 1972.]