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EDITORIAL

# Ibuprofen safety at the golden anniversary. A commentary and recent developments

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**Abstract**

Ibuprofen is a long lasting non-steroidal anti-inflammatory drugs (NSAIDs) and still represents one of the most diffused analgesics around the world. It has an interesting story started over 50 years ago. In this short comment to an already published paper, the authors try to focus some specific important point. On top, they illustrate the recent, confusing and fake assertion on the potentially dangerous influence that ibuprofen could have, increasing the risk of Coronavirus infection. This is also better illustrated in a previously published paper, where the readers could find more clear responses to eventual doubts.

**Keywords**

NSAIDs; Ibuprofen; COVID-19; Side effects

## 1. Introduction

The passing of Stewart Adams (Fig. 1) inspired the publication of an interesting paper on the "golden anniversary" of ibuprofen [1], whose inventor had been the mentioned great Pharmacist [2].

He had joined the Boots Pure Drug Co., Ltd. in the 1950s and had started immediately to study new analgesics for rheumatoid arthritis. The initial studies on the new molecules had brought the productive group of scientists to synthetize over 200 new compounds, of which only 5 had the chance to be studied clinically. Ibuprofen was one of them. Patented in 1961, it was cleared to the UK medical market in 1969. Its safety profile allowed the drug to be sold over-the-counter (OTC) very soon [1].

Last year, the use of this analgesic, in use for over 50 years, has been questioned about its safety, especially for its administration in patients affected by infectious diseases [2]. The French National Medicine Agency, reporting 49 cases on millions of patients using this medicine, was concerned that existing infections could be worsened by the use of NSAIDs, and especially of ibuprofen [3].

## 2. Ibuprofen characteristics

A review article on ibuprofen safety has reconfirmed its safety profile and has shown how efficacious this medicine is also as anti-febrile [4]. Moreover, its balanced, non-selective cyclo-oxygenase inhibitory activity reinforce the already known properties of the drug, which is basically a universal anti-inflammatory, anti-febrile, and especially analgesic product fitting many necessities. Of course, there are many other products, more selective that can be useful for specific pathologies or patients' necessities, but it is indisputable that ibuprofen is safe, and has extremely well-known side effects, mainly gastro-intestinal, like any other drug of its class [5]. Compared to other OTC analgesics, ibuprofen showed a better safety profile in a recent study analyzing several medicines [6]. Also, in a meta-analysis comparing over 1,000 patients receiving ibuprofen with over 1,000 patients treated with paracetamol, the frequency of adverse events was similar in the 2 groups [7]. Similar results have been demonstrated in a different study comparing paracetamol, acetyl-salicylic-acid (ASA) and ibuprofen, with a favorable safety record for the latter [8]. Finally, a comprehensive overview of systematic reviews has analyzed the safety profiles of OTC analgesics [9]. It has shown that the incidence of side effects attributable to some of them, including ibuprofen, was similar to placebo, when used at recommended doses, to treat acute pain for few days [9].

The anti-febrile effect of ibuprofen has never been questioned till recently, at the beginning of the COVID-19 pandemic. In fact, very surprisingly Le Figaro Sciences on March 14, 2020, referring to a social media information diffused by a high level France politician (*March 14, 2020, tweet of Dr. Olivier Véran, France Minister of Health, recommending to avoid any anti-inflammatories and to prefer paracetamol, in case of fever for COVID-19*), diffused the alarm against anti-inflammatories, and especially against ibuprofen, asserting that their use could be connected to serious COVID-19 infections [10]. Scientifically, the information was supported by a "Correspondence" published on Lancet Respiratory Medicine. The scientific article presented an interesting theory on the necessity to change therapy to patients in treatment with ACE-inhibitors and/or ibuprofen [11]. Immediately after, it has been criticized because of its scientific inconsistency [12]. Actually,


  

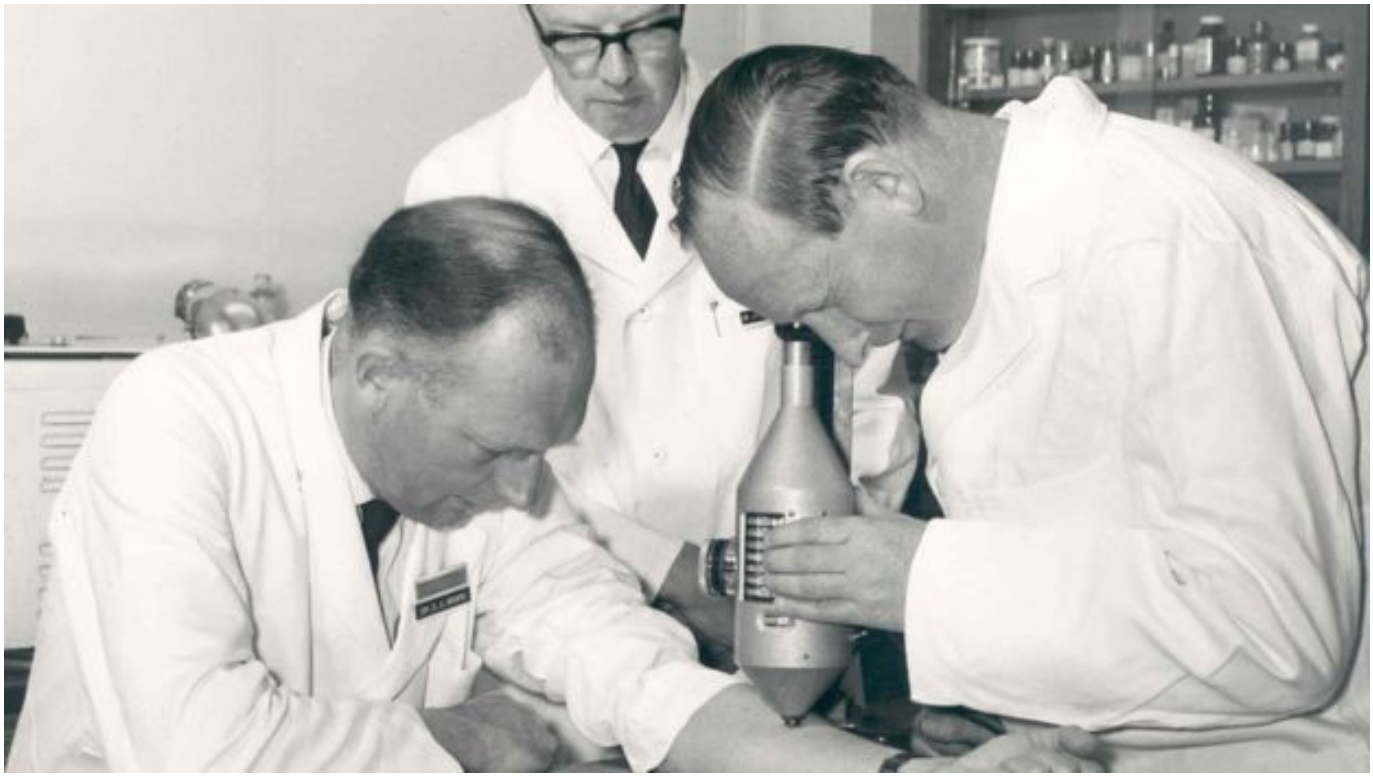

**FIGURE 1. Stewart Adams and his Colleagues, studying the degrees of inflammation on themselves.**

the theory expressed by Fang *et al.* [11] did not have any data in support, and even worse, the opinion appeared in Dr. Olivier Vértan's tweet, previously mentioned, was not logical from the pathophysiologic point of view. The inflammatory syndrome, frequently at the basis of severe cases of COVID-19 infections, may only have some benefit from the use of anti-inflammatory drugs. In fact, more recently the information arriving from Dr. Vértan, and reported on The Guardian Health, are in opposite direction: anti-inflammatory drugs are strongly recommended to prevent in children inflammatory syndrome potentially linked to Coronavirus infections [13].

That said, in our opinion a good doctor or scientist should never forget the logic, and the basic concepts of human pathophysiology, especially in moments of emergency medicine. In such conditions, it might become dangerous to try to "build castles in the air", and/or to find a topic that could become a "bone of contention", in order to increase the visibility.

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## CONFLICT OF INTEREST

Giustino Varrassi is in the editorial board of several scientific journal. Both authors do not have any other potential conflict of interest to declare.

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