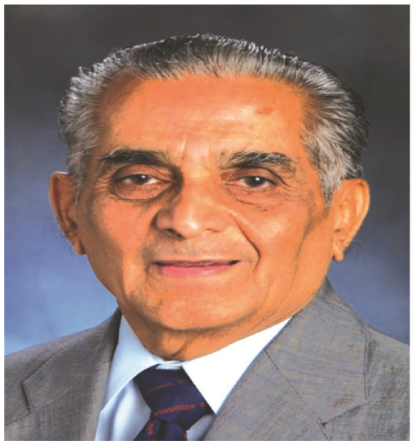
M. C. Wani (1925–2020)

The legendary organic chemist Mansukh Wani passed away at the age of 95 on 11 April 2020, at Durham, North Carolina, USA. He was born in 1925 at Nandurbar, Maharashtra, India, and earned graduation and post-graduation degree from the University of Mumbai in 1947 and 1950 in the Organic Chemistry respectively. After completion of his Ph D in Chemistry from Indiana University at Bloomington in 1962, Wani moved to the University of Wisconsin at Madison, USA, for his postdoctoral training. After that, he joined the Research Triangle Institute (RTI) at Research Triangle Park, North Carolina, and remained there till the last moment of his life.

Wani was a follower of Mahatma Gandhi and involved in many freedom fights, particularly the famous satyagraha movement of Nandurbar, Maharashtra.

Wani's core strength in research was isolation, characterization, crystallography and total synthesis of biologically active natural products. Wani and his group were the first to report the isolation, characterization, X-ray crystal structure and antitumour activity of camptothecin. They have isolated it from stem wood of *Camptotheca acuminata*, *Nyssaceae* and established its anticancer activity[1]. Together with Monroe Wall, he developed the crystal structure of Camptothecin and developed other potent water-soluble derivatives of Camptothecin. These pioneering discoveries led to the development of potent derivatives of these drugs (irinotecan and topotecan from Camptothecin, and Paclitaxel and Docetaxel from Taxols). Continuing their search for potent anticancer agents from natural sources, Wani and his team established the isolation, characterization and antitumour activity of taxol from the stem bark of the western yew, *Taxus brevifolia*. At this time, it was the first compound possessing the taxane ring with anticancer and antileukemic activity[2]. Besides identifying the novel anticancer agents from natural sources, Wani and his group have developed many potent derivatives of camptothecin through the total synthesis route. They found that 20(*S*)-camptothecin derivatives bearing the 9- and 10-substitutions were most active in *in vitro* as well as *in vivo* compared to other derivatives[3]. Besides the identification of novel compounds, Wani has established the mechanism of action of these compounds. For example, he was the first to establish the molecular mechanism for camptothecin antitumour activity and showed that it inhibits an essential enzyme, topoisomerase-1, by binding at enzyme-DNA interface. He proved his hypothesis by synthesizing 7-chloromethyl and 7-ethyl derivatives of camptothecin. Further, few synthetic derivatives of camptothecin, such as soluble 20(*S*)-glycinate esters of 10,11-methylenedioxycamptothecins were evaluated and established the structural



activity relationship among these analogues[4–7]. The journey for the discovery of taxol and camptothecin was nicely presented in one of his articles where he had discussed all aspects of drug discovery, starting from the collection of plant material, biological screening, isolation of natural products and finally, established the therapeutic efficacy in animals[8].

He also reconfirmed the therapeutic efficacy of the betullnic acid using bioassay-guided fractionation obtained from the methanolic extract of the stem bark of *Ziziphus mauritiana* Lam. (Rhamnaceae). This pentacyclic triterpene induces selective cytotoxicity in melanoma cells through the induction of apoptosis[9]. During his scientific career, he had published more than 300 research articles and obtained 36 patents for the discovery of novel compounds for the treatment of cancer and other diseases. He was the first Indian scientist who has discovered two anticancer drugs from natural products.

Wani's work came up with two (taxol and campothecin) clinically used drugs for cancer treatment. This satisfaction is reflected from his quote, 'Nothing could be more gratifying than this. I have always been interested in the study of chemistry to develop medicines, and I am very proud of our accomplishments.'

Wani has received many international honours and awards including Bruce F. Cain Memorial Award from the American Association for Cancer Research, the City of Medicine Award by the Greater Durham Chamber of Commerce, the National Cancer Institute Award of Recognition, Charles F. Kettering Prize from the General Motors Cancer Research Foundation, the Ranbaxy Research Award from the Ranbaxy Science Foundation, Distinguished Alumni Award from Indiana University, and a plaque commemorating the discovery of Taxol by the Gifford Pinchot National Forest of Washington State. In 2003, he was recognized by the American Chemical Society for the discovery of Camptothecin and Taxol at RTI. Further, in 2005, he was awarded by the Governor of North Carolina with the North Carolina Award in Science. He received the Paul Ehrlich Magic Bullet Lifetime Achievement Award in 2008.

Besides a great scientist, Wani was a humble human being and always ready to help and support young scientists for their future endower. We remember him for his generous support and informative lecture at Saurashtra University, Rajkot, India (1998) to PG students, research scholars and faculty members. Recently in 2018, A.K.S. visited him at his North Carolina residence. Wani was pleased to see him and shared his gratitude and showed him his latest award, 'World Changer', for his contribution as co-inventor of two drugs. He also shared his story about losing priority for Taxol synthesis because his research was published in the public domain before his patent application.

It will be appropriate to celebrate his memories by creating a small archival museum by keeping his research notes, memories, personal literature, photographs, awards and citations (which can be obtained from his family and RTI). The ideal location of this museum may

M. C. Wani and Monroe E. Wall who discovered jointly two important drugs Taxol and Camptothecin.

be either at his native place, Nandurbar, or at the University of Mumbai to inspire the future generation.

He left behind his wife, Mrs Ramilaji, son, Bankim, daughter-in-law, Darshana; and grandson, Nilesh. We thank Dr Jitender Bariwal and Priyanka Desai for help in the preparation of this writeup.

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