Real World Example of Green Chemistry Practices in an Indian Industry

Preview

Ranitidine HCl is an important and cost effective antiulcerant available to the people of India and many other countries. The total production of Ranitidine HCl by Indian Pharmaceutical Industries is more than 50% of the world requirement (4000m tones annually).

Hazards in the Manufacture of Ranitidine HCl

In the process of manufacturing of Ranitidine dimethyl sulfide is generated that is not only detrimental to the health and environment but also has a strong obnoxious odour. The pharmaceutical companies manufacturing this drug are encountered with an acute problem in dealing with the situation. Many such industries go for incineration of methyl mercaptan thereby destroying the compound but polluting the environment with SOX. Due to the problems originating from dimethyl sulfide many manufacturers were served with closure notice by the Pollution Control Boards. Indeed some of the major manufacturing companies were compelled to shut down the production for several months causing severe shortage of the medicine in the market.

Green Chemistry Initiative leading to the Practical Solution

Taking cues from the work of Professor Mihir K. Chaudhuri of IIT Guwahati, Dr. M. Lakshmi Kantam of IICT, Hyderabad and their coworkers (Sanjay K. Dehury, B. Neelima, Ch. Venkat Reddy) supported by the knowledge gained from the sustained research of the former (MKC) on peroxo-metal chemistry, newer catalysts have been designed to achieve a Green Process for the production of the Ranitidine HCl. The functional catalysts have been developed jointly by RCHEM Pvt. Ltd. Hyderabad and Professor Mihir K. Chaudhuri of IIT Guwahati. The heterogeneous catalysts that have been put on to use for the commercial production of the drug are based on Vanadium-Titanium or Titanium-Phosphorous compounds. Using hydrogen peroxide as the oxidant, the catalysts convert dimethyl sulfide with obnoxious odour to dimethyl sulfoxide (DMSO), a odorless and colorless liquid. DMSO that is generated is used in the manufacturing process of the drug thereby reducing the cost production by 20%. A win-win situation for the industry through the adaptation of Green Chemistry tenets.

Catalytic Method for conversion of foul smelling toxic gases like methyl mercaptan generated in the manufacture of ranitidine base (daftmen base), and similar emissions from other drugs/intermediates to useful by-products recyclable in the same process.

Ranitidine HCl is a commonly used anti ulcer drug. Six or seven industries produce Ranitidine HCl in INDIA with the total production amounting to a little over 50% of the global requirement. SMS Pharmaceuticals Ltd. located at Hyderabad in India is the largest manufacturer of Ranitidine HCl. They sell this product in India and export in a good quantity. Importantly, in the process of production of this drug, a large quantity of methyl mercaptan is generated in the plant. Methyl mercaptan is a low boiling liquid that rapidly turns into gas at ambient temperature and pressure having obnoxious odour of rotten cabbage. The low vapour density of the gas facilitates its easy diffusion into and rapid mixing with the atmospheric air thereby rendering the air stinky. Moreover, methyl mercaptan is a health hazard because it causes dizziness, headache, nausea, respiratory arrest, and even coma and unconsciousness. A little longer exposure to high concentration of the gas can be fatal. The sustained contact with liquid or the gas may cause frostbite as well.

Owing to the fact that methyl mercaptan gas spreads quite fast over wide area and contaminates the ambient air in addition to creating nuisance with foul and hazardous smell lingering for hours together, this requires to be controlled by proper treatment at the site of production itself. Several industries in India are encountered with this problem and the issue has become a matter of great public concern. In order to maintain the atmosphere clean, green and sustainable, this has to be quantitatively controlled.

The current practice in the concerned industries is incineration, a process has several drawbacks. It not only produces flue gases like sulfur dioxide but also needs scrubbing, and the cost of production is quite high any way. An associated problem with incineration is maintaining the combustion rate. Each time this needs to be regulated in order to match with the volume of emissions. And this happens especially because the gas

emission is not uniform since the drug synthesis is conducted as a batch process. Scrubbing of the emitted gas with alkali solutions could be another way of tackling the problem, however, this is accomplished by a very high cost involved in treating the spent solutions. Alternatively, adsorption on activated charcoal could be yet another possibility but recycling of the adsorbent is a polluting process. In view of the scenario presented above many pharma industries including Nuland Laboratories, Dr, Reddy's Lab., Saraca Laboratories and SMS Pharmaceuticals Ltd. have been grappled with the problems especially since they practice incineration. Indeed some of the Ranitidine HCl manufacturing industries including SMS Pharma Ltd. and Saraca Labs. located at the suburbs of Hyderabad had to close down their production units due to the enforcement of environment protection legislations. Evidently, such industries have been desperately and frantically looking for a solution to this problem as well as to reduce the cost of production of this life saving drug.

In a significant development, SMS pharmaceuticals Ltd. of Hyderabad and Professor Mihir K. Chaudhuri of IIT Guwahati have come up with an improved protocol to render the manufacturing process of Ranitidine HCl clean and environmentally benign. What has been done is that metyl mercaptan has been first converted to dimethyl sulfide that is catalytically converted to the odorless dimethyl sulfoxide (DMSO) in a quantitative manner. Over two decades of research experience of Professor Chaudhuri of IIT Guwahati in the area of oxidation chemistry and the industrial experience of Mr. P. Ramesh Babu and Mr. T.V. Srihari of SMS Pharma Ltd. and Mr. Suresh Babu of RCHEM Ltd. have led to this success. While H_2O_2 is the terminal oxidant, the newer catalysts are based on titanium, vanadium, aluminum and a solid acid in one case. The catalytic process has been assigned to RCHEM Pvt. Ltd. at Humnabad for green production of Ranitidine HCl for SMS Pvt. Ltd. The catalytic process has been in use for over the past one year for commercial production of the drug. Important is also to note that the DMSO produced by the catalytic reaction is used in the process itself thereby reducing the total cost of production by nearly 40%. A WIN WIN situation indeed. This is a real world example of "Green Chemistry and Green Technology" practice in India.

A catalytic industrial process for conversion of methyl mercaptan, foul smelling toxic gas, to value added odorless dimethyl sulfoxide.

Role of Green Chemistry Network Centre, Delhi University

Having been inspired by the on going activity of the Green Chemistry Network Centre at DU, Mr. T. V. Srihari, Technical Director of RCHEM Pvt. Ltd. invited Dr. R.K. Sharma to visit the production unit of RCHEM Pvt. Ltd. located at Humnabad, Karnataka. Accordingly, the production site was visited on 10 September 2006 to look into the facilities and the plant in operation, peruse the chances of gas leakage, if any, and the eventual possibilities ecologically objectionable waste production. Incidentally, Dr. D. C. Sharma, Addl. Director, Central Pollution Control Board (CPCB) and Mr. M. D. N. Sinha, Chief Environment officer, Karnataka State Pollution Control Board (KSPCB) also visited the production unit on the same day (photograph enclosed). Mr. T. V. Srihari made a detailed presentation of the process technology, while Professor Mihir K. Chaudhuri explained the entire chemical technology including the catalytic greening of the process. Dr. R. K. Sharma and the CPCB and KSPCB experts were all extremely pleased to get the first hand information and to see the "Green Process" in operation. In addition, the industrial premise was found to be very neat, clean and well maintained, no obnoxious odor was felt, let alone that of methyl mercaptan, and no objectionable waste production was observed.

KUDOS TO SMS Pharma and RCHEM FOR ADOPTING GREEN CHEMISTRY and CLEAN TECHNOLGY CULTURE IN THEIR INDUSTRIES. IT IS INDEED A VERY GOOD REAL WORLD EXAMPLE OF GREEN CHEMISTRY PRACTICES IN AN INDIAN INDUSTRY