Organic and Medicinal Chemistry
International Journal
ISSN 2474-7610

Juniper Publishers
key to the Researchers

Letter to Editor
Volume 2 Issue 4 - May 2017
DOI: 10.19080/OMCIJ.2017.02.555591

Organic & Medicinal Chem IJ

Tertiary Care in Impurity Trends New Pattern Discovery: Letter to Editor

Rahul Hajare*[1,2]

[1]*Department of Quality Assurance, Rajgad Dnyanpeeth's College of Pharmacy, India*

[2]*Former Post-Doctoral Fellow, Indian Council of Medical Research Department of Health Research Former Post-Doctoral Fellow, India*

Submission: May 08, 2017; **Published:** May 15, 2017

***Corresponding author:** Rahul Hajare, Department of Quality Assurance, Rajgad Dnyanpeeth's College of Pharmacy, Indian Council of Medical Research Department of Health Research Former Post-Doctoral Fellow, India, Tel: 91-9765704048; Email: rahulhajare@rediffmail.com

Letter to Editor

Impurity in pharmacopeia has been accepted as a non-clinical agent that can be kept under control, however difficult to eliminate. The hope for possible zero impurity has stemmed from the reports of the methods at high risk of impurity transmission remaining free in spite of repeated exposures to the reaction. A number of molar and non-molar factors associated with lower susceptibility to impurity transmission and better control on impurity multiplication have been reported. This has been a significant barrier in developing effective treatment against impurity entrapment. On the contrary, a spectacular success has been achieved in the field of pharmaceutical impurity treatment. A large number of methods in multiple solutions based on their mechanisms of action have become available and sustained pressure from chemical society across and initiatives by international pharmacopeial standards have been successful in taking the free treatment to majority of those who require it Anti-impurity treatment has made it possible for impurity processed product to lead a normal product by keeping impurity multiplication under control for a long time, thus effectively making impurity a chronic that can be kept under control by long treatment.

This has been possible due to availability of alternatives as the non-aqueous solvent and other solvents system and other line of solvents. Although researchers looked for (zero impurity) cure, the impurity reservoir in the process development of chemical drugs is difficult to eliminate. Different approaches are currently being followed in an attempt to stimulate the impurity and mopping up the resultant impurity particles before they have opportunity to entrap new product and establish reservoir. There was a shot in the arm for cure research with the presentation of a case of 'functional cure' by Roy J et al. [1] at the Conference on Biomaterial USA and New Development in Organic Chemistry Hageriearly this year. A new born to impurity positive raw material was put on the anti-impurity treatment within 12 h of analytical report. The positivity status of the new born impurity was confirmed both by UPLC as well as by CNMR. The new born impurity when retested after 48 h of anti-impurity treatment was found to be negative for impurity. The new born impurity continued to be negative after withdrawal of anti-impurity treatment. The investigators claimed a "functional cure" in the impurity. This finding was very significant as this functional cure was achieved by administering molar warm demineralise water first anti impurity treatment, which are part of the first line treatment for impurity transmission throughout the product development. This may make it a feasible strategy for functional cure. With this report further impetus was given to the research for cure from pharmacopeial impurity. In this issue, Hogerzeil HV et al. [2] reports a possible cure in a new born to impuriy positive raw material. To the initial level impurity was diagnosed to be impurity based on major raw material and minor raw material.

The test was performed in a private R & D analytical laboratory accredited by National Accreditation Board for Testing and Calibration Laboratories (NABL). The results were confirmed by repeat testing. At 30 days the impurity was tested for standard impurity and was found to be negative. The negative status was confirmed by again UPLC and CNMR, repeat spike impurity for standard impurity and quantitative. The authors have considered a possibility of elimination of impurity as a result of anti-impurity treatment. These findings raise the issue related to early control of impurity multiplication. A short period of 3 days after the exposure to impurity is called an "Eclipse phase" during which there is no impurity detectable in circulation. This period may also be very important in deciding whether the aqueous solvent responses will limit the impurity. By the time the impurity appears in the final drug it may have already spread to different particles of drug and established in the product. Once the impurity is established it is difficult to eliminate the impurity. Hoq MM [3] initiated the anti-impurity treatment within 60 h of detection and may have prevented

establishment of the impurity reservoir in the product. Peter J S [4] have initiated the treatment after eclipse phase was over and hence it will be difficult to explain how established impurity was eliminated. In "Cohort", recently impurity products were treated with anti-impurity treatment as late as 3 weeks after detection. The treatment was stopped after up to4 months of treatment. After the treatment was withdrawn the product continued to have no detectable impurity.

The investigators called these as "post-treatment impurity controller" Ahuja S [5]. Hence the claim by Ahuja S, et al. [6,7] cannot be dismissed merely on technical context. It is possible that along with anti-impurity treatment the impurity response of the early born impurity may have eventually helped in clearing drug impurity reservoir. The Authors themselves have been cautious in their interpretation and have not ruled out false positive results in NMR. Although the two cases are similar, there are distinct differences in the two reports. While the initial step was put on anti-impurity treatment within36 h in the product development study the new born impurity in study by Roy J, et al. [1] was put on the anti-impurity treatment after 72 h. One of the limitations brought out by the investigators is that the detection in the new born impurity was not confirmed by UPLC and NMR. In this study impurity occurs when warm demineralize water has avoided from the synthesis and showed that impurity level increases or decrease significantly after a poor compliance of water. Water combined with reaction mixture used to treat co - associated impurity in process development, when multiple solvent may be used, there is possibility of more exothermic and under rated relevant for impurity and its interaction, which drag them and come along with product development with impurity way. Also purity or limits of impurity and its coping measurements for drug products present a challenge to pharmacopeial standards-setting of a drug product over time is at issue. If the findings reported by Hoq M M, et al. [3] are further confirmed in larger chemical studies, the new ICH guidelines would probably pave way for impurity free next generation drug. Hence these findings are extremely significant and need to be followed by larger and controlled studies. The paper will indeed generate discussion on this important advancement [8-10].

Reference

1. Roy J, Islam M, Khan A H, Das S C, Akhteruzzaman M, et al. (2001) Diclofenac Sodium Injection Sterilized by Autoclave and the Occurrence of Cyclic Reaction Producing a Small Amount of Impurity. J Pharm Sci 90: 541-544.
2. Hogerzeil HV, Battersby A, Srdanovic V, Stjernstrom N E (1992) Stability Of Essential Drugs During Shipment To The Tropics. British Medical J 304: 210-214.
3. Hoq M M, Morsheda SB, Gomes DJ (1991) Bang J Microbiology 8(1): 5-9.
4. Peter J S, Ahmed A, Yan W (2006) An HPLC chromatographic reactor approach for investigating the hydrolytic stability of a pharmaceutical compound. J Pharm Biomed Anal 41: 883-890.
5. Ahuja S (1998) Impurities Evaluation of Pharmaceuticals. Marcel Dekker, New York, USA.
6. Ahuja S (1992) Chromatography of Pharmaceuticals: Natural, Synthetic and Recombinant Products. ACS Symposium Series 512: 7-25.
7. Ahuja S, (1997) Chiral Separations by Chromatography, Oxford University Press, NY, USA .
8. Federal Register (1997) International Conferences on Harmonization. Guidance for Industry: Impurities Residual Solvents, U.S. Department of Health and Human Services Food and Drug Administration (CDER) Q3C 1-13: 27.
9. Walker GJA, Hogerzeil HV, Hillgreen U (1988) Lancet 2: 393.
10. Food and Drug Administration for immediate release consumer media (1998) 888-Info-FDA.

DOI: 10.19080/OMCIJ.2017.02.555591

How to cite this article: Rahul Hajare.Tertiary Care in Impurity Trends New Pattern Discovery: Letter to Editor. Organic & Medicinal Chem IJ. 2017; 2(4): 555591. DOI: 10.19080/OMCIJ.2017.02.555591