



Classical R & D and Laboratory Practises of 8-Methoxy-5-(Morpholin-4-ylmethyl)-4,4a,5,9b-Tetrahydro-1H-Pyrazino[2,3-B] Indole-2,3-Dicarbonitrile

Rahul Hajare

ICMR NARI PDF Batch-2013-15 National AIDS Research Institute, India

Post-Doctoral Fellow 7 th Indian Council of Medical Research, New Delhi

Ph. D Scholar Batch-2007-12 Vinayaka Mission University

Abstract

Industrial R & D is known for its post attraction after receiving a minimum qualification to get a job in research and development. Due to ever –increasing failure rates, high cost, unsatisfactory safety profile and limited efficacy associated with production of drug. It is also seen most of the R & Ds are convert production base R & D. When we work on any drug in research development we started the thinking of government policies rather than a result. Actively supports a full range of research focused on using innovation to develop practical solutions to key industry issues - including new product development and commercialization. R & D may be better known in the industry for its work in the field of certification, but it is activity as a research & development (R&D) centre in gemmology has been no less significant. Today, it is the only full-fledged research laboratory in field of gemmology in India, is very difficult recognised as a research certification laboratory. Well equipped with the most sophisticated instruments, R&D department is on par with many international laboratories, having wide ranging capabilities in different aspects of gemmology. Classical laboratory R & D is a platform to create a research mind in small spaces with negative result is best result in research that can improve the research hand and capabilities. We practiced economical laboratory R & D in small space. Here we investigated laboratoty drug through classical R&D of synthetic new drug in minimum sophisticated analytical tools and instrument.

Keywords. R & D, Direct Process, Pilot Batch, Process Development and Trial Batch Run

Language: English

Date of Submission: 2018-03-05

Date of Acceptance: 2018-04-10

Date of Publication: 2018-04-30

Volume: 01 Issue: 01

Journal: To Chemistry Journal

Website: <https://purkh.com>



This work is licensed under a Creative Commons Attribution 4.0 International License.



R & D tree has design the below diagram

Charge Round Bottom Flask-100ml



Addition of 5-Chloro Isatin 0.007M



Charge Morpholin 0.007M/Piperidine 0.007M



Catalytic amount of Formaldehyde (0.3 g, 0.01 M)



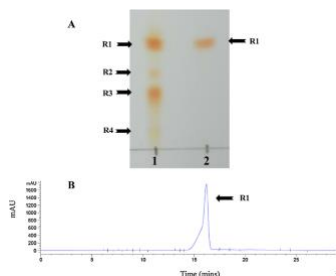
Reflux Ethanol 20 ml



Stirring 40-45^o C/for 2 hrs



Check TLC every 10-15 minutes of interval (TLC of reaction mass)



sitting 30 min





Stage 6

Charge N-Morpholinomethyl Indole 2,3, dione 0.002M



Reaction with 4-Pyridinecarbohydrazide 0.002M



Treatment with Glacial acetic acid 2 ml



Charge with 40 ml ethanol



Check TLC

Reflux with stirring 1 hrs

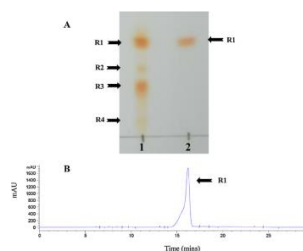


Check TLC

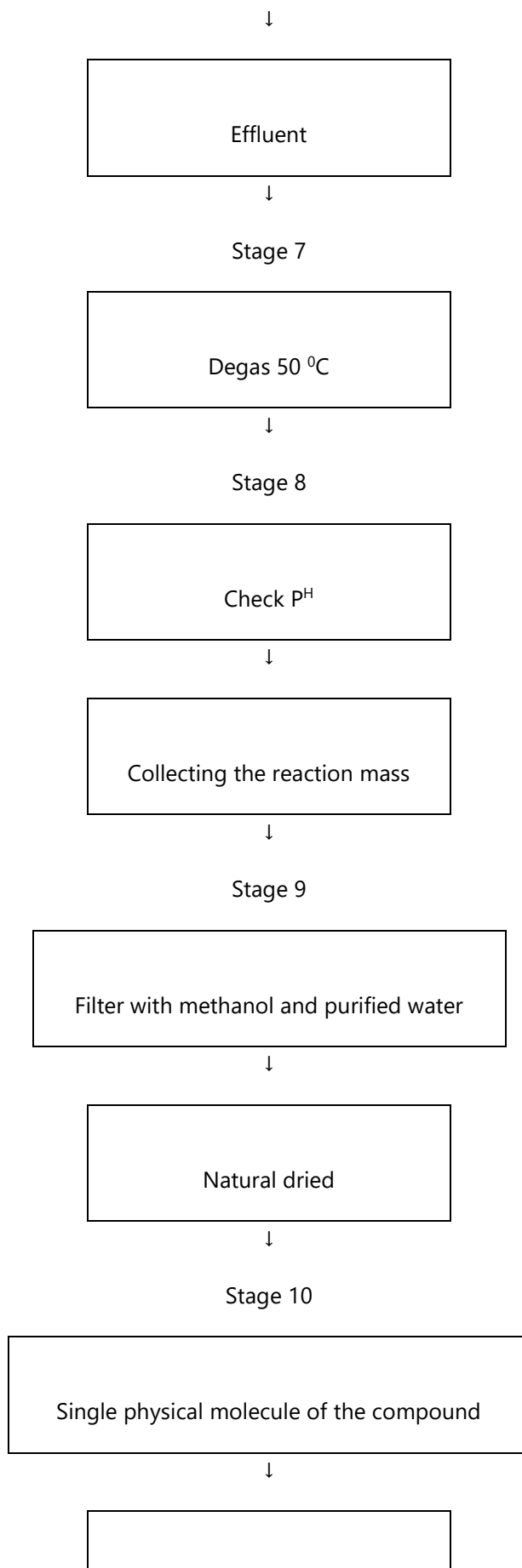
Charge Round Bottom Flask

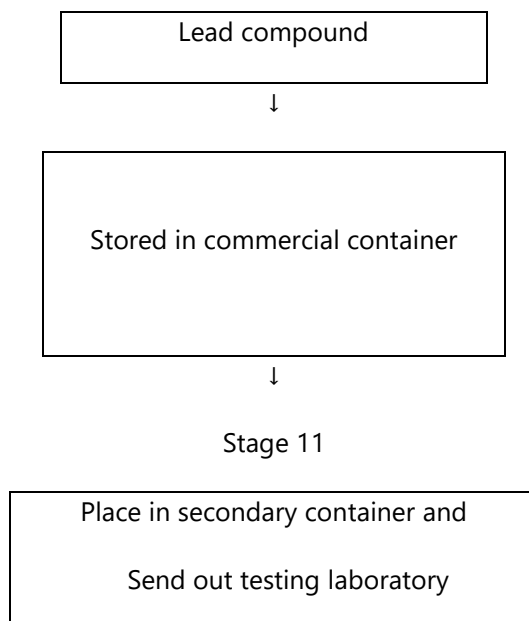


Check with TLC



sitting 30 min





Trial batch

Cleaned 100 ml round bottom flask, charged 1.85 g, 5-Chloro Isatin, and charged 0.3 g, formaldehyde, charged 0.6 g morpholin, charged ethanol (20 ml) was stirred for the period of 1 h. The batch temperature was maintaining gradually 30^o, 40^o, 50^o and hold 60^o-65^o for 30 min to complete conversion in 2-4 hrs (1, 2). The mixture was then refluxed for 4 h or till the completion of reaction (as confirmed by TLC). Then the reaction mixture was cooled and poured in ice cold water. The obtained was filtered and recrystallized using ethanol. Lead *N*-morpholinomethyl-indole-2, 3-dione: To 0.002M of *N*-morpholinomethyl isatin, equimolar quantity of diaminomaleonitrile and 0.5 ml of glacial acetic acid were added and refluxed in 50 ml of ethanol for 2 hours on water bath. Excess of ethanol has been pooling since first stage and was removed and after drying (3,4), the compounds were purified from ethanol. Synthesized of different 5-(morpholin-4-ylmethyl)-4,4a,5,9b-tetrahydro-5-substituted-1*H*-pyrazino[2,3-*b*] indole-2,3-dicarbonitrile. 8-methoxy-5 (morpholin-4-ylmethyl)-4,4a,5,9b-tetrahydro-1*H*-pyrazino[2,3-*b*] indole-2,3-dicarbonitrile. Filtered reaction mass at room temperature and caked washing by 10 ml ethanol. Calculate wet weight. Dried at 60^o-65 C in oven for 3 hrs and collected dry weight.

Pilot batch

Bypass simplified direct process for manufacturing of lead 8-methoxy-5-(morpholin-4-ylmethyl)-4,4a,5,9b-tetrahydro-1*H*-pyrazino[2,3-*b*] indole-2,3-dicarbonitrile has overcome the difficulties associated with spray drying of product. Unless indicated otherwise, all percentages referred to herein has on a weight (w/w) basis. The reagents involved in the production of lead compound have 5-chloro isatin diethyl part and morpholin required quantity. Concentrated formaldehyde is commonly 85% in ethanol; however, other percentages may be used. Concentrations between about 70 and may be used. 85% (weight /volume or weight/weight) may be used. Concentrated formaldehyde has used at concentration of about 40-50%. Both reagents have combined into a reaction vessel. The reagents may be pumped into the reaction vessel or manually added. Pumping of each reagent has occurred at a variety of rates. Depending on the size of the reaction tank, the reagents have pumped into the reaction tank. Ethanol has added to dilute the reaction mixture and to maintain slurry. Once both reagents have added, the reaction mixture usually has mixed for a period of time, usually about 10, 20, 30, 60, 120 or more minutes (5,6). Mixing can occur by a variety of mechanism. One common method of mixing is to use agitators have operate at a variety of speeds to obtain the most efficient mixing, to prepare the *N*-morpholinomethyl-indole-2, 3-dione. Then transport *N*-morpholinomethyl-indole-2, 3-dione as a raw material adding 4-pyridinecarbohydrazide into to reacted for 4-5 hrs under the temperature ranging from 50-



55 °C (7,8). After the reaction has been mixed it has transferred to a storage tank where it has combined with additional same lead compound reaction mixture from separate reactions and allowed to cool to crystallize. Usually, the reaction mixture has cooled to about 60 °C or lower, often about 55 °C or 50 °C or lower. The reaction mixture may be cooled by any means of refrigeration commonly used for chemical mixtures or the reaction may be allowed to cool without the assistance of any means of refrigeration. Once the reaction mixture has been cooled it then may be homogenised. This reduces the particle size within the cooled reaction mixture/slurry. Any suitable equipment may be used such as an IMPLEX high shear mill homogenizer set at about a 25-micron clearance between the rotor and stator (9, 10). The reaction mixture has pumped into the homogenizer and collected in a storage container such as a stainless-steel drum. Any means of pumping may be employed. For example, a peristaltic pump has used to move the cooled reaction mixture to the homogenizer. After the reaction mixture has homogenized, an additional peristaltic pump has used to move the homogenized slurry to a spray dryer. Spray drying involves the atomization of a liquid into a spray followed by the drying of droplets in a drying chamber. When the moisture evaporates from droplets, dry particles have formed and these particles have released from a drying chamber for collection. Spray dryers usually have a feed pump, an atomizer, an air heater, an air disperser, a drying chamber and system for exhaust air cleaning and powder recovery. One example of a spray dryer that may be used is a 16 ft. diameter nitro spray dryer. However, other types of spray dryers may be used. The mixture/ slurry have passed directly to the atomizer at an appropriate rate. The inlet temperature has sent to a temperature between about 300 °C and 500 °C and the outlet temperature has set to a temperature between about 90 °C and 105 °C often the outlet temperature has between about 90 °C and 100 °C and the inlet temperature has between about 350 °C and 400 °C. Many factors have involved in determining particle size such as the degree of atomization, the concentration of the solution, and the degree of homogenization. Any one or more of these factors have manipulated to alter particle size. The resulting product has generally a free-flowing powder of lead compound 8-methoxy-5-(morpholin-4-ylmethyl)-4,4a,5,9b-tetrahydro-1*H*-pyrazino[2,3-*b*] indole-2,3-dicarbonitrile that has typically in the particle size range of about 75-100 microns. However, it should be understood that the particle size has deviate from exemplified range.

Production

Production and perception calculated in tones.

It is a mathematical function that relates the maximum amount of output that can be obtained from a given number of input- generally capital, labour in large scale.

Conclusion

To understand these phenomena, and to predict performance in the particular circumstances, requires detailed new models. Such models and the system parameters needed within them can be generated using commonly available equipment and software. Warming up of earth due to pollution has due to greenhouse effect. In both cases energy retention in green house has caused by lack of convection that has lack of mixing of the interior air with the surrounding atmosphere. So green house may thus become considerably warmer than the temperature of the surrounding atmosphere higher of the concentration of CO₂ more of outgoing IR radiation will be absorbed and more will be reradiated back to earth surface. This will be increasing the earth's surface (green house temperature) temperature with increase in CO₂ concentration in air. Classical research and development laboratory practices will help to shrink carbon footprint. Additional author emphasis on the framing of well-planned strategy to responsible for reduce carbon footprint.

Recommendation:

Based on the findings of our study, the following recommendations are suggested: To shrink carbon footprint:

a) Eat a plant-based diet, b) Avoid air travel, c) Don't drive a car and d) Have a small family



Acknowledgements

This study has been guided under the supervision and guidance of **Renowned Laboratory Scientist Respected** Dr. Ramesh Paranjape, Retired as Director & Scientist 'G' National AIDS Research Institute, India. I express my deep gratitude towards Respected Sir for motivation and being great knowledge source for this work.

Conflict of Interest

Authors do not hold any economic interest in this work, and they do not hold any conflict of interest.

Reference:

1. Rahul Hajare, Smita Kulkarni, Madhuri Thakar and Ramesh Paranjape, Technology Development and Design of Novel 1, 3, 5-tri Substituted-1H-Indole-2, 3-Dione HIV-1 Inhibitors with Displays Strategic Nanomolar Cytotoxicity. *World J Pharm Pharm Sci.* 2016; 5(6): 391
2. Rahul Anandrao Hajare, Smita S. Kulkarni, Ramesh Shivram Paranjape, Design Space Filling Model, Synthesis and Evaluation of Novel 2-Indolinone HIV-1 Inhibitors. *International Journal of Advanced Research.* (2015), Volume 3, Issue 12, 1332 – 1335.IF:4.5
3. *Hajare R (2018) New Technology of Nucleoside AIDS Virus Resistance Drug Key Intermediate Diethyl (Tosyloxy) Methylphosphonate. J Virol Antivir Res 7:1.*
4. Rahul Hajare, Response to a 2 Indolinones laboratory based regimen analogous in cancerous-infected cells. *Biomed Res Ther* 2017, 4(S)
5. Rahul Hajare. Classical Technology Can Run Away Impurity in Pharmaceuticals Frugal Innovation Lesson from Classic Innovation System. Opinion article (2017), *Organic & Medicinal Chem IJ.* Volume 2 Issue 4: DOI: 10.19080/OMCIJ.2017.02.555592.
6. Rahul Hajare, Tertiary Care in Impurity Trends New Pattern Discovery: Letter to Editor. (2017), *Organic & Medicinal Chem IJ.* Volume 2 Issue 4 DOI:10.19080/OMCIJ.2017.02.555592.
7. Rahul Hajare, Characterization of Inconsistent Unspecified Impurity Associated with Specified Impurity and Adjacent to Other Detectable Impurities Who Have Not Listed in Pharmacopoeias in Ciprofloxacin Hydrochloride. (2017), *Chemical Sciences Journal: Volume 8 • Issue 3: 1-3*
8. Rahul Hajare, E-IPA-Encyclopedia of Impurity Profile (IP) for API, (2017), *The Pharma Innovation Journal;* 6(1): 05-06
9. Rahul Hajare, Matrix Impurity, Disregards Impurity, Specified Impurity Associated Undetectable Impurity: Monograph, *World J Pharm Pharm Sci.* 2016; Volume 6, Issue 1, 242-246
10. Rahul H, pre_DR Technology. (2016) *KJACT-100106* Volume 2, Issue 1 -3